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# STREPTOMYCIN COMBINED WITH SURGERY IN THE TREATMENT OF BONE AND JOINT TUBERCULOSIS

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Reports on the effect of streptomycin in the treatment of tuberculosis of bones and joints for the most part have been inconclusive or unpromising.[1] Apparently most patients were treated with the antibiotic alone, without concomitant surgical measures. Brock,[2] Morgan and Bosworth [3] reported success with streptomycin in the treatment of tuberculous sinuses. Bickel and others [4] described 16 cases with streptomycin therapy, some in conjunction with fusion procedures, with 9 good results. These included 2 good results in synovial tuberculosis of the knee without surgical operation. Pulaski and associates [5] treated tuberculosis in 24 cases, 18 of the spine and 6 of the extremities, with 6 good results. Michele and Krueger reported success in 12 cases with the use of both streptomycin and surgery.[6] The largest and most carefully studied series of cases, with the best results, was that reported by Bosworth and others.[7]

The purpose of our study was to determine the effect of streptomycin in conjunction with definitive surgical procedures, either extirpation of the lesion or arthrodesis, in the treatment of an unselected series of patients with tuberculosis of bones and joints. It is recognized that the effect of streptomycin is bacteriostatic [8] and that it would be too much to expect the drug to exert a direct effect on advanced lesions with destruction of tissue, caseation and fibrosis.[9]

From the Clinic of the New York Orthopaedic Dispensary and Hospital.
Read before the Section on Orthopedic Surgery at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

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## MATERIAL AND METHOD

*Clinical Material.*—Thirty patients were treated at the New York Orthopaedic Dispensary and Hospital between March 1947 and December 1948. Two of these were discarded from the study because they did not meet all the stipulations, but they did contribute interesting side lights, which will be mentioned in the course of the report. Of the remaining 28 patients, 15 had disease of the spine, with two areas involved in 2 cases; 4 had disease of the hip, in 1 combined with a spinal lesion; 3 had tuberculosis of the knee, 2 of the elbow and 2 of the foot, and 2 had tuberculous abscesses secondary to lesions of the spine and hip, which had been treated years previously by arthrodesis. There were 15 adults from 21 to 58 years of age and 13 children aged 4 to 17. Twelve patients were male and 16 female; 20 were white and 8 Negro. The cases varied from those of long-standing infection with a low order of activity to comparatively recent, acute infections with pronounced activity. Thus, although the number of cases is small, they represent a cross section of various types of infection.

*Follow-Up Period.*—The follow-up period from the beginning of combined treatment varied from four months to two years, with an average of more than one year for the majority. It thus is evident that this is only a preliminary study and that years must elapse before the final result can be determined. However, it is possible to state the immediate effect of the combined treatment on these patients. In the majority an arthrodesis was obtained, a fact which gives us some confidence in the eventual outcome of treatment. The validity of the diagnosis, a most important point in any study of tuberculosis of bones and joints was established by pathologic tests in 20 cases. The evidence in the other 8 cases, 7 of the spine and 1 of the hip, as furnished by the history, roentgen ray and other laboratory tests, was so convincing as to leave little doubt.

*Determination of Streptomycin Dosage.*—At the beginning of the study there was comparatively little data to guide us in deciding the dose of streptomycin which would be most effective. Dihydrostreptomycin sulfate was not then available, and we used streptomycin calcium chloride complex.[10] In the first cases 2 Gm. of streptomycin was given intramuscularly daily in six to eight doses, with injection of an additional 1 Gm. in a sinus or abscess if one was present. It soon became evident that toxic symptoms, usually manifested by vertigo or nausea, would develop relatively early with this dosage, and the amount was reduced to 1 Gm. daily for adults and 0.5 Gm. for children under 12 years of age.[11]

*Vestibular Disturbance.*—In only 1 patient in this series was there a slight residual vestibular impairment. It was still present after twenty months. This patient received only 58 Gm. of streptomycin in twenty-three days, with a daily dose of 2 Gm. intramuscularly and 1 Gm. locally. In 8 other patients transient vestibular symptoms of varying degrees developed, usually after the fourth week of therapy. A reduction in the dosage or a temporary suspension of the drug invariably relieved the condition. In a few instances streptomycin was continued in the same amounts in the face of slight vestibular

10. A large part of the streptomycin for this study was donated by Merck & Co., Inc.
11. We are now administering 2 Gm. of dihydrostreptomycin sulfate daily for adults.

disturbance without further impairment. Not infrequently an incorrect interpretation of the patient's complaint and of the result of the Kobrak test may have been responsible for some of the contradictory phenomena. There was no patient with auditory disturbance attributable to the drug.

*Eosinophilia.*—In about 70 per cent of the patients examination of the blood revealed a rise of 3 to 9 per cent in the differential eosinophil count beginning at the fourth week of therapy for a varying period to the sixteenth week. In 1 patient in this series there was an increase of eosinophils to 13 per cent at the fourth week. This patient made an excellent response to the combined streptomycin and surgical therapy. Some patients who did well had no increase in eosinophils. It is difficult to correlate the phenomenon of eosinophilia with the clinical progress of the disease, but it was not associated with adverse effects in any of the patients.

*Other Manifestations.*—Cutaneous eruption was observed in only 1 patient on the seventh day of therapy. This is the patient in whom eosinophilia (13 per cent) developed at the fourth week. The relationship here is highly conjectural. With a reduced dosage of streptomycin the cutaneous rash disappeared in a few days. Contact dermatitis had not been observed.

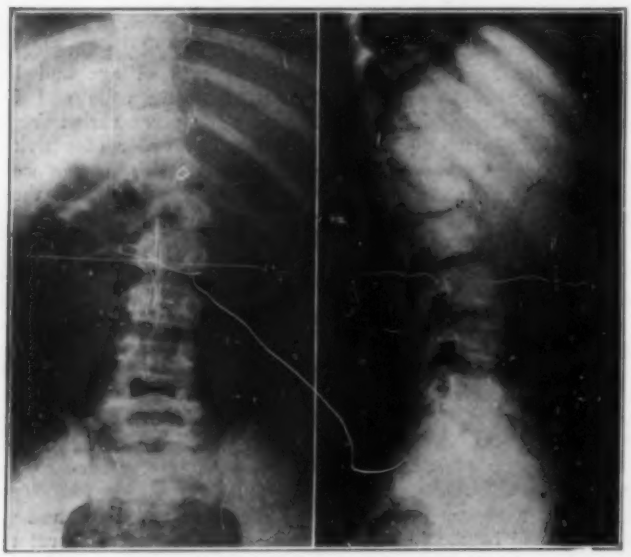

Fig. 1.—Destructive lesion of the first lumbar vertebra of three months' duration in D. S., a girl 12 years of age, Aug. 15, 1946; similar lesion barely discernible between the fifth lumbar and the first sacral vertebrae.

One patient in this series had a low grade fever (around 100 F.) throughout the course of treatment. The temperature returned to normal as soon as administration of streptomycin was discontinued, at the end of the prescribed period.

## RESULTS OF THERAPY

In the estimation of the effect of streptomycin in conjunction with surgical measures, it must be remembered that the results of spinal fusion or arthrodesis of other joints alone has been highly effective in a large percentage of cases in the past and that only if results are obtained which are definitely better than we could expect from surgical procedures alone are we justified in giving credit to streptomycin. With this taken into consideration, we believe that there is striking evidence in these cases that in certain conditions streptomycin exerts a remarkable influence on the disease. This was particularly so in toxic, active, rapidly progressing infection in which rest and surgical intervention could not be expected to, and indeed did not, retard the inexorable progress of the disease. Following is the most dramatic example of this.

D. S., a Negro girl aged 12 years, with tuberculosis of the first lumbar vertebra of three months' duration, was admitted to the hospital Aug. 27, 1946 (fig. 1). Because of her high temperature and sedimentation rate and her evidently toxic condition, she was kept in bed and various means, including blood transfusions, were used to improve her condition. In spite of this she rapidly became worse, lost her appetite and became apathetic. Although we would have preferred to postpone surgical intervention, it was thought that the only chance of arresting the disease was in doing a spinal fusion. This was attempted Jan. 13, 1947, five months after her admission to the hospital. It was found that in addition to the body of the first lumbar vertebra the posterior arch was involved and

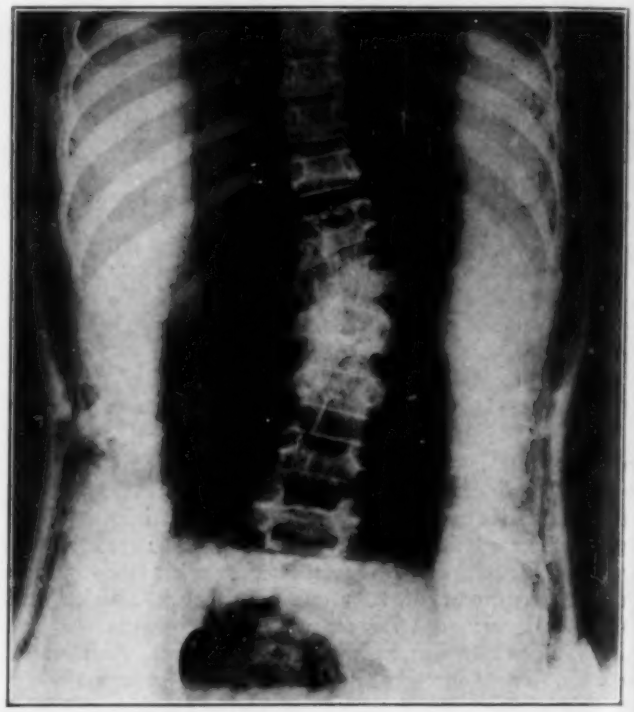

Fig. 2.—Roentgenogram March 12, 1947, two months after fusion of the twelfth dorsal to the second lumbar vertebra. Streptomycin had not yet been given; destruction is now apparent in the twelfth dorsal vertebra.

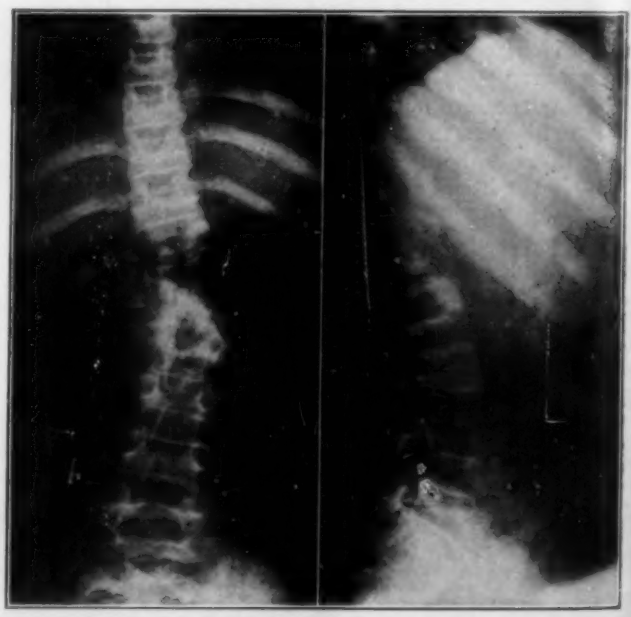

Fig. 3.—Views of spine May 16, 1947, two months after institution of streptomycin therapy and four months after spinal fusion. Note that the disease appeared arrested in the twelfth dorsal and first lumbar vertebrae with recalcification, while the process went on unabated between the fifth lumbar and the first sacral vertebrae, for which fusion had not yet been performed.

that there was a dorsal abscess. A sinus formed after the surgical operation, and the condition of the patient became worse.

On March 19, 1947 it was decided to try streptomycin therapy. At that time the temperature was high, the sedimentation rate was decidedly increased and the girl was emaciated. Roentgen examination showed progressive destruction of bone and no evidence of fusion (fig. 2). Within one week after streptomycin therapy was started her temperature fell, her appetite returned and she began to take an interest in her surroundings and to gain weight. The sinus closed within a short time, and the abscess subsided. The improvement in her condition continued with drop in temperature to normal and lowering of the sedimentation rate. It was discovered that a second lesion was present in the fifth lumbar vertebra, and, although the roentgenogram showed recalcification of the dorsolumbar lesion and unmistakable evidence of fushion, the lumbosacral focus did not show a corresponding improvement (figs. 3 and 4). A lumbosacral spinal fusion was performed Nov. 24, 1947, and fusion occurred uneventfully with apparent arrest in the progress of the lesion (fig. 5). The patient was discharged from the hospital March 1, 1948 and has shown no evidence of recurrence of the disease.

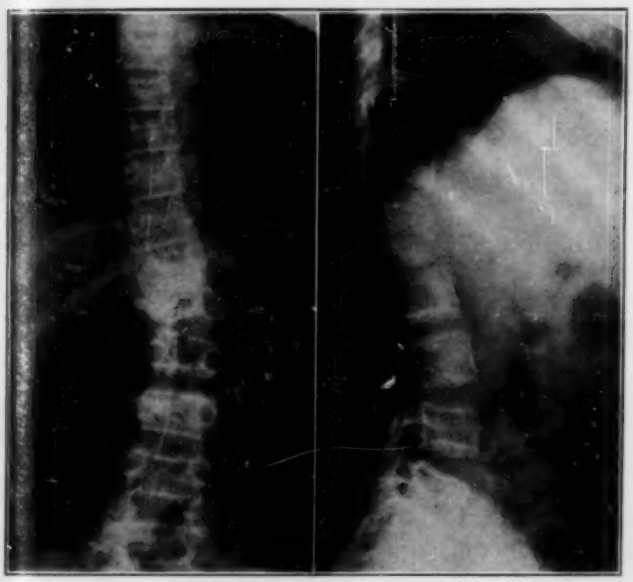

Fig. 4.—Roentgenograms Nov. 10, 1947, eight months after streptomycin therapy and ten months after fusion of the twelfth dorsal to the second lumbar vertebra. Note further consolidation and repair of the twelfth dorsal and first lumbar vertebrae and progressive destruction of the fifth lumbar and first sacral vertebrae.

In a similar case a Negro woman aged 28 had disease in both cervical and lumbar segments of the spine. The cervical portion of the spine was treated first under the combined regimen with good response, but the lumbar lesion deteriorated until that segment was fused and a second course of streptomycin therapy was given three and one-half months after the cervical fusion. These 2 cases afforded an unusual opportunity to observe the behavior of simultaneous lesions in two isolated segments of the spine, one lesion treated by streptomycin and surgery and the other by streptomycin alone. The latter did not heal until a surgical fusion was performed, whereas the former in each instance quickly subsided.

In a third case the result was almost as striking.

L. S., a girl 9 years of age, with a destructive lesion in the left hip, had a daily elevation of temperature and a sedimentation rate (Westergren) of 60 mm. The Mantoux reaction was strongly positive. She was kept in bed with traction on the left leg, but there was no improvement in her condition and roentgen examination showed rapidly increasing destruction of the hip (fig. 6). A fusion of the hip was performed Jan. 12, 1948. Exceedingly active disease was found, with advanced destruction of the femoral head and acetabulum, and there was an abscess. Streptomycin therapy was begun on the day of operation. Her general condition rapidly improved, and there

Fig. 5.—Three months after fusion of the fifth lumbar to the second sacral vertebra, Feb. 16, 1948. Note that disease is arrested in the fifth lumbar and first sacral vertebrae and there has been further repair of the twelfth dorsal and the first lumbar vertebrae.

was clinical and roentgenologic evidence of solid fusion on Dec. 15, 1948, eleven months after operation (fig. 7). The plaster spica was removed December 15, and she was discharged from the hospital December 21, one year after admission.

Fig. 6.—Roentgenogram Dec. 18, 1947, showing acute disease of left hip with lesion in femoral neck in a girl aged 9 years. Extensive destruction and abscess were found at operation.

It is certain that such a result could not have been obtained in these cases without the use of streptomycin, and we are reasonably sure that it could not have been brought about by the use of streptomycin alone.

The results obtained with streptomycin in the treatment of abscesses with or without sinus also have been striking. We now do not hesitate to incise a tuberculous abscess and to inject streptomycin daily if aspiration and injection cannot be performed effectively.

One of our earliest cases was that of a Negro with tuberculosis of a sacroiliac joint, complicated with a large abscess. The man was emaciated, had a high temperature and sedimentation rate and loss of appetite. He seemed dangerously ill. The abscess was aspirated but promptly refilled. At the third aspiration streptomycin was injected into the cavity, and systemic administration of the drug was begun with a dose of 2 Gm. daily. The abscess subsided after two additional aspirations and injections, and it remained healed after twenty-six days of therapy. Meanwhile the general condition of the patient improved remarkably. His temperature and sedimentation rate fell, the former to normal, his appetite improved and he gained weight. He left the hospital at the end of two months, refusing to have a sacroiliac arthrodesis.

Another patient with an abscess in the region of the greater trochanter, twenty-three years after a successful fusion of the hip for tuberculosis, had excision of the abscess followed by injection of streptomycin into the wound daily as well as intramuscular injection of 2 Gm. of the drug each day. Streptomycin therapy was discontinued after sixteen days because vertigo developed, but the wound healed promptly at the eleventh postoperative day; there had been no recurrence of the abscess at the end of twenty months.

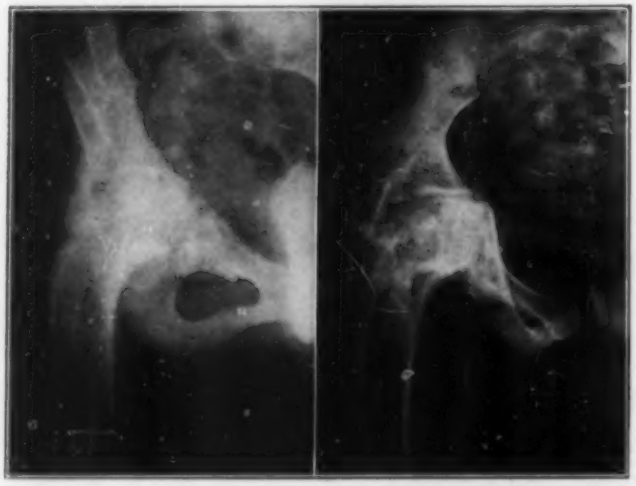

Fig. 7.—Views of hip Dec. 15, 1948, eleven months after combined therapy. Note the firm union of the graft and intra-articular consolidation.

A woman aged 46 had multiple tuberculous lesions of the spine, including one in the dorsal region, each of which was treated by spinal fusion; a right subpectoral abscess developed, which gradually increased in size and which finally was dissected out six years after the dorsal spinal fusion. It was possible to remove the abscess cleanly back to the axilla, but there a large sinus tract was found leading posteriorly, deep to the axillary structures. The wound was closed except for a small catheter, through which 1 Gm. of streptomycin was injected daily; 2 Gm. of the drug was also given intramuscularly. The catheter was withdrawn, and the wound healed in twelve days; there has been no evidence of recurrence of the abscess after two years. This is the patient (mentioned previously in the section on Vestibular Disturbances), who has mild, persistent vertigo.

The outcome was less favorable in a Negro woman, aged 28, who had multiple sinuses in the left lumbar and right hip regions with abscesses in the left lumbar and trochanteric areas. The abscesses were incised and drained, and streptomycin was introduced into the sinuses and was given systemically. The immediate result was good, but the sinuses reopened and drained. Although an extensive roentgenologic search was made, we could not determine with any certainty the focus of the infection and therefore were unable to deal with it effectively. Hense, this case was not included in the series.

The evaluation of the results in this series is based on: (1) the rapidity with which the joint becomes fused under treatment; (2) the absence of further extension of the disease process; (3) a rapid return of calcification of the bone wtih distinct outline; (4) the prevention of complication by abscess and sinus formation or the healing of preexisting abscess or sinus, and (5) an alleviation of symptoms and improvement in the general well-being of the patient.

There were 3 definite failures among the 28 cases studied. Two were cases of tuberculosis of the spine.

A Negro man 46 years of age had tuberculosis of the sixth and seventh dorsal vertebrae with involvement of the posterior arches and a paravertebral abscess. Spinal fusion failed to occur after operation, and a second attempt was made to repair the defect. Because of beginning paraplegia a costotransversectomy was performed. Streptomycin was given intramuscularly, but treatment with the drug soon was discontinued because of urinary observations indicating nephritis following a transfusion reaction. Streptomycin therapy was resumed, and a total of 118 Gm. was given without any apparent beneficial result. On Nov. 7, 1948, one year after the first spinal fusion operation, tuberculous meningitis developed. Streptomycin was given again but had no apparent effect, and the patient died Nov. 17, 1948.

The other failure among the spinal cases was in a white man aged 50, who had had a laminectomy performed at another hospital because of paraplegia. An extradural abscess was opened, which proved to be tuberculous. Streptomycin was given, the patient was later transferred to this hospital, where spinal fusion was attempted three months after the laminectomy. Meningitis developed two months after the second operation; the man was transferred to another hospital, where he died.

It is thought that the administration of streptomycin to these 2 patients over a period of time before the development of meningitis may have resulted in the appearance of a streptomycin-fast strain of bacteria.

Failure thus far also has been the result in a girl 11 years of age who had extensive involvement of the right hip with decided destruction of the ilium above the acetabulum. She was kept at rest in bed for three months, and a Brittain arthrodesis was then performed with the institution of streptomycin therapy, which was continued for forty-two days. In spite of a revision of the arthrodesis, union failed to result. However, it may well be that this was due to faulty operative technic.

Among the 13 remaining spinal cases, 3 patients had compression of the cord with paraplegia before operation and quadriplegia developed in 1 after fusion of the cervical portion of the spine. Two of the first 3 patients were found to have extradural abscesses, but the third patient did not undergo further surgical exploration. This patient recovered fully after streptomycin therapy and spinal fusion, and 1 of the others has improved sufficiently to be up and around. The other 2 are improving. Results in these 13 patients, 9 of whom had acute or subacute disease and 4 chronic, were rated as follows: 10 excellent, 1 good and 2 fair. The 2 patients considered as having only fair results were so judged because of the persistence of paraplegia, although the spinal fusions were solid and the condition of the patients otherwise was improved. The sinuses in all these patients healed and still were closed at the last examination.

All 4 cases of tuberculosis of the hip occurred in children from 6 to 14 years of age. Two were in the acute stage of the disease with duration of eight weeks and of ten months. Active infection was found in the joints at operation. The third child had extensive disease of the acetabular roof involving the hip, and the fourth child required refusion because the hip had failed

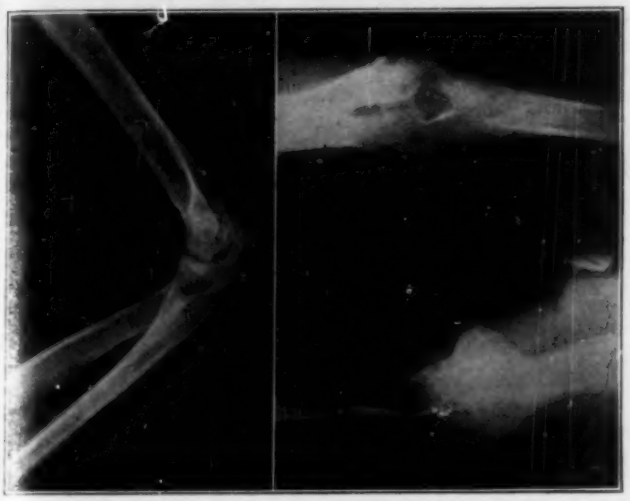

Fig. 8.—Roentgenogram May 18, 1947, showing chronic disease of the elbow of nineteen years' duration in a woman aged 26.

to ankylose eighteen months after the primary fusion and there was a draining sinus of one to two months' duration in the region of the hip. The results in 2 of the 4 hips are considered excellent. One was the acutely infected hip previously described. In spite of the activity of the disease, no sinus formed after operative treatment. In the other case, in which a refusion was performed, the graft became solid six months after operation and the sinus healed in three months. In 1 of the remainder, as was mentioned in the preceding paragraph, fusion failed to occur after an ischiofemoral arthrodesis, probably because of faulty technic. The fourth patient, who had an acute infection of the hip of ten months' duration, is doing well, four months after operation, with healing of a sinus. However, it is too early to evaluate the final result.

The three cases involving the knee are of particular interest. All patients had extensive synovial involvement, and in 1 there was disease of the upper end of the patella but no other evident lesion of the bone. All 3 patients were treated by synovectomy, with excision of the upper fourth of the patella in 1. Administration of streptomycin was started intramuscularly just before operation in each case and was continued for an average of eight weeks. It was injected into the knee prior to operation in 1 instance, but such a severe reaction resulted that the local injection was not repeated in this patient or in the other 2. Motion of the knee was begun at the end of two weeks. In all these patients the swelling, heat and tenderness gradually subsided postoperatively and had disappeared in a period of six to ten weeks. The recovery of motion was slow, and it was not forced. The patients were encouraged to perform active exercises, but forcible passive motion was not carried out. It was thought best not to risk trauma which might reactivate the infection; as long as motion was recovered eventually, we were content to have it return slowly.

The disease was extensive in all these cases, and the synovium was firmly adherent to the capsule and medial collateral ligaments, making it difficult to remove without damaging these structures. It obviously was impossible to remove all the diseased tissue, but we hoped that the streptomycin therapy would be effective in sterilizing the balance. So far there has been no evidence of infectious activity, but these patients especially must be observed for a period of years before there is any certainty that they are cured.

The response of the 2 patients with tuberculosis of the elbow is considered excellent. An arthrodesis was performed in 1 and resection of the elbow in the other. The patient with arthrodesis of the elbow gave a history of infection of nineteen years' duration, during which several surgical operations had been performed eleswhere for drainage, to gain motion and to restore neural function. After a protracted effort had succeeded in closing a persistent sinus about the elbow, it was fused according to Hallock's technic.[12] Fusion took place in three and one-half months without postoperative sinus formation (figs. 8 and 9). The other patient with tuberculosis of the elbow gave a history of two years' duration with persistent draining sinus. Because of extensive destruction of the area it was decided to resect the elbow together with the diseased synovium. The sinus closed two weeks postoperatively, and the elbow remained asymptomatic to the end of a four month follow-up period.

In 1 of the tarsal cases there was extensive destruction of the mediotarsal area and proximal metatarsals. The sinus is healed and the focus appears inactive, although the patient is now being treated in a sanatorium for a pulmonary lesion. The other patient, who had involvement of the subtalar joint, had a good fusion without sinus formation five months after treatment.

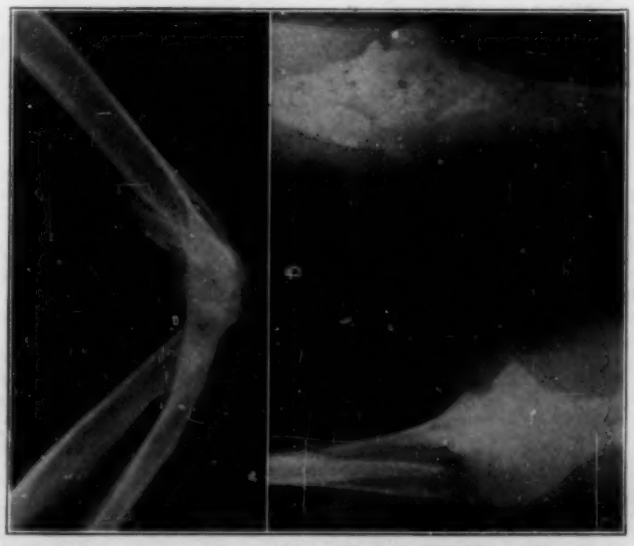

Fig. 9.—Same elbow Dec. 15, 1947, three and one-half months after fusion and streptomycin therapy. It is solidly fused.

The extent to which streptomycin exerted any favorable influence on the course of the chronic, relatively inactive infections, uncomplicated with abscesses or sinuses, is difficult to determine. The course of some of these patients after surgical intervention did not differ essentially from that which would have been expected from surgical measures without streptomycin therapy.

12. Hallock, H.: J. Bone Joint Surg. 14: 145, 1932.

SUMMARY

1. Streptomycin in conjunction with definitive surgical procedures, such as excision of the lesion or arthrodesis of the affected joints, was used in 28 cases of tuberculosis of bones and joints at the New York Orthopaedic Dispensary and Hospital.

2. The period following the termination of treatment is too short to make possible other than a preliminary report, but it is evident that streptomycin exerted a decidedly beneficial influence on active, acute infections. A number of patients with these infections recovered and attained a solid arthrodesis within a surprisingly short period.

3. Tuberculous abscesses and sinuses responded quickly to combined streptomycin and surgical therapy.

4. Three cases of synovial tuberculosis of the knee joint were treated by synovectomy and streptomycin. The early results are favorable.

CONCLUSIONS

1. Streptomycin combined with definitive surgical procedures has a striking effect on active tuberculous infections of bones and joints and undoubtedly makes it possible to perform operative measures in these cases much sooner than they otherwise could be done, thus preventing long periods of invalidism and extensive destruction of the joints.

2. Tuberculous abscesses and sinuses arising from infections of bones and joints heal promptly under the influence of streptomycin, provided the primary focus is dealt with surgically at the same time.

3. The influence of streptomycin on chronic, more inactive tuberculous lesions of bones and joints is not easily determined, because patients with such lesions usually do well with surgical intervention alone. It may be unwise to administer streptomycin in such instances because of the possibility of making the organisms streptomycin-resistant, thus rendering the drug ineffective if it should be needed at some future time.

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## ABSTRACT OF DISCUSSION

Dr. Charles N. Pease, Chicago: This detailed study by Drs. Smith and Yu, reporting uniformly good results with combined streptomycin and surgical therapy along with an equally gratifying report made recently by other investigators, firmly establishes this antibiotic as an absolute essential in the treatment of tuberculosis of bones and joints. My use of streptomycin has been limited almost wholly to tuberculosis of the bones and joints in children, and here it has been of inestimable value. Now that streptomycin is available to everyone, I look for the possibility of a confused picture in establishing proved cases of tuberculosis of bones and joints. I cite the following case in point. A girl aged 5 years was sent to the Children's Memorial Hospital Nov. 5, 1948 by an orthopedic surgeon who had made a clinical diagnosis of tuberculosis of the right hip. The onset was in July 1947, but the child was not seen by the surgeon until one year later. She was placed in a spica cast in July 1948 and given 0.33 Gm. streptomycin for sixty days. The cast had been removed after three months, but local symptoms persisted in the hip. On admission to the hospital there appeared to be activity of the disease, with a high degree of involuntary muscular rigidity fixing the thigh in 30 degrees of flexion and 5 degrees of adduction with only 10 degrees of motion to rotation at the hip joint. There was a history of contact. The Mantoux reaction was positive. On Nov. 30, 1948, a suprapubic extraperitoneal right obturator neurectomy was performed, followed immediately by combined intra-articular and extra-articular fusion. Although clinically and roentgenologically this was a case of tuberculosis of the hip (and even if it were not), the changes had advanced to such a degree that treatment could not be expected to result in a good, movable, painless hip. However, synovia and bone removed at the time of the operation showed a healed inflammatory process. No evidence of tuberculosis could be recognized microscopically. It may be that a representative specimen was not submitted to the pathologist, or the sample of tissue might have been from a formerly tuberculous area which had healed.

Dr. Paul W. Hugenberger, Boston: This is a preliminary report based on a small number of patients, both with acute and with chronic infections, between the ages of 4 years and 58, with a follow-up period far too short to formulate definite conclusions. I would hesitate to give streptomycin to patients with chronic, quiescent or healing infections without draining sinuses, in which the immediate results of surgical procedures alone are so satisfactory; moreover, it is known that solid bony fusion does not insure against future reactivation of the tuberculous process and that the giving of streptomycin unnecessarily might result in the production of streptomycin-resistant bacteria, thus making future treatment ineffectual. One must also bear in mind the possibility of toxicity. At the New England Peabody Home for Crippled Children in Newton, Mass., a few acute infections (6) have been treated in infants under the age of 2 years with relatively large doses of streptomycin for relatively short periods, with encouraging results; they have not been followed long enough to determine end results. Before streptomycin was used, we had the highest mortality in this age group; so far, since streptomycin has been given, there has not been a death. All these infants have shown decided improvement in their tuberculous lesion roentgenologically within a four month period following onset of treatment, and in 1 case bony fusion seemed to have taken place between the second and third lumbar vertebrae. A patient 1 year and 2 months of age, with symptoms for three months in the right hip, was given streptomycin for nineteen days with definite improvement clinically and by a roentgenogram taken two months later, and with pronounced improvement six months after the start of treatment. Another patient, 1 year and 3 months of age, with seven distinct lesions of bones and joints (four in the spine, two in the shoulders and one in the ankle), with a cervical abscess and pulmonary involvement, was given streptomycin intramuscularly, with aspiration and injection of streptomycin into the cervical abscess; there was definite clinical improvement. These patients are all too young for surgical arthrodesis. They are entitled to a fairly long period of conservative treatment following streptomycin therapy, but they will not require the prolonged, more rigid immobilization which they would otherwise have needed. I wonder what Dr. Smith or Dr. Yu would recommend for treatment in these infants? I agree with them that internal fixation by fusion carried out at the proper time is the treatment of choice in the older age group and that surgical measures can be performed earlier and more safely with concomitant streptomycin therapy.

Dr. Timothy C. H. Liang, Cassadaga, N. Y.: At Newton Memorial Hospital, Cassadaga, N. Y., 240 patients have been treated with streptomycin during the past thirty-four months; 18 of them have tuberculosis of bones and joints, either single or multiple sites of involvement. The result of the treatment is most dramatic. One patient had a huge psoas abscess, 2 had paravertebral abscesses; all showed disappearance of the abscesses in four to six months. Two had sinuses of elbows and 1 of the costochondritis. The closure of the sinuses occurred in three to six weeks. One patient with multiple communicated and serpiginous sinuses of the hip of nine years' duration showed closure of all sinuses after streptomycin treatment plus sequestrectomy of her right ileosacral joint. Four patients with spinal lesions showed good bony ankylosis of the spine in less than two months after additional fusion or grafting operations.

In 1 white girl aged 13, with bilateral severe tuberculosis of the hip joint, the process was completely arrested without bony ankylosis of the joints; in addition, the active pulmonary tuberculosis was arrested. She is able to walk like a normal child except for a ½ inch (1.3 cm.) shortening of the right leg. A white girl aged 4 years had disease of the left hip joint and pathologic fracture of the distal part of the femoral neck, with

dislocation of the head upward. After streptomycin therapy, in six months the fractured ends showed solid bony reunion in rectangular angle. A thick, strong, bony pseudoacetabulum was formed at the site just above the original acetabulum, where the head of the dislocated femur is in place. The new pseudojoint showed good bony ankylosis. It is interesting to observe that these patients with tuberculosis of bones and joints showed rapid bony ankylosis in a comparatively short time and that they had no recurrence of active disease even eight to twenty-six months after completion of streptomycin therapy.

DR. DAVID M. BOSWORTH, New York: Drs. Smith and Yu do not know completely what the end results will be. The situation is in a state of flux and can only be determined by a mass of material carefully studied, and a lifetime is hardly long enough for that study. Streptomycin has an action far beyond its inhibitory one on the tubercle organism. Its most outstanding action is the dramatic change it causes in the physical condition of the patient, without any regard to local lesion. It provides the surgeon clinical material which is operable. It appreciably decreases spread, locally or otherwise, of the tubercle organism. The wide spreading of the incisional areas which break down with tuberculosis organisms is infrequently seen when streptomycin is given for a couple of weeks in advance of surgery. In closed cases the action of the drug is nowhere near as dramatic as in those with sinuses. There it is truly a life-saving drug. My associates and I have had a series of patients who in ninety days received 90 Gm. of the drug, and we have taken sections of tissue from them. In all we have found evidence of active tuberculosis on smear, culture or section. Included were 2 patients with tuberculous knees, 1 patient with a tuberculous elbow and 1 patient with a tuberculous tibia. In only 1 instance has biopsy shown no evidence of residual tuberculosis. That patient had a tuberculous hip and had received 697 Gm. streptomycin parenterally and 51 Gm. intrathecally for meningitis. The proper treatment of patients with these tuberculous lesions becomes the duty of an institution with strong financial backing. The patients are frequently impoverished, and for the prolonged care and observation needed a considerable amount of money is necessary. The city of New York at Sea View Hospital is expending about $150 a day for streptomycin for patients with tuberculosis of bones and joints. That is over $45,000 a year. It would be impossible for us to make an adequate study were there not such places to provide the opportunity to investigate, treat and rehabilittate these destitute and unfortunate persons.

DR. ALAN DEF. SMITH, New York: I have emphasized that this is only a preliminary report. However, I regard the effect of streptomycin as short-lived and temporary, so I believe we have had a good opportunity to see what the drug will do within a limited time. I do not think that it can be expected to have any long-continuing result. The drug simply enables the surgeon to operate on patients whom he otherwise would not be able to treat surgically, and it affects the course of the disease during the brief period while it is given, so that surgical treatment has a better chance to succeed. We still depend fundamentally on surgery and not on streptomycin.

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**Phlebothrombosis.** — Deep phlebothrombosis of the lower extremities continues to be a problem far reaching in its complications and sequelae. Its importance is readily indicated by the fact that fatal embolism following phlebothrombosis occurs in 3 to 6 per cent of cases. Further, 11 to 18 per cent of patients who survive one pulmonary embolus experience a subsequent one which is fatal. Chronic lymphedema is another serious problem not to be taken lightly. It is evident that the most desirable treatment is that which will result in a minimum of swelling, reduce morbidity and avoid mortality. In spite of the voluminous literature now listed on the subject some misunderstanding apparently still exists as to the indications for femoral vein section and especially the levels for section.—L. H. Eisendorf, M.D., Phlebothrombosis of the Lower Extremities, *The American Journal of Surgery*, October 1949.

## FIBROCYSTIC DISEASE OF THE PANCREAS

### Treatment by Sympathetic Denervation of the Pancreas and Presentation of a Theory of Neuroeffector Mechanisms: Preliminary Report of Five Cases

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Since recognition of fibrous replacement of the acini of the pancreas associated with severe nutritive and respiratory disease as a pathologic and clinical entity in 1938,[1] remarkable advances have been made in the treatment of pancreatic fibrosis, which has resulted in prolonging the life of these patients. Such treatment has been primarily dietary, supplementary and prophylactic against recurrent and intercurrent infections. This has resulted in extension but not alteration of the uniformly fatal prognosis of this disease.

A new method of treatment consisting of sympathetic denervation of the pancreas by splanchnic block with procaine hydrochloride and complete splanchnicectomy on the right side has been employed by us in 5 cases with spectacular immediate results. These cases together with the presentation of a theory of neuroeffector mechanisms form the basis of this report. The diagnosis in each of our cases was established by demonstration of absence of pancreatic enzyme (trypsin) in the duodenal contents.[2] Indirect confirmation was offered in all cases by histories, physical examinations and fecal analyses and in 3 cases by flat vitamin A tolerance curves. Splanchnic blocks were performed according to a modified Kappis technic,[3] 5 to 10 cc. of a 1 per cent solution of procaine hydrochloride being used, depending on the size of the child. General anesthesia with vinyl ether was necessary because of poor cooperation in these young patients with local anesthesia alone. Splanchnicectomies were accomplished through infradiaphragmatic approaches. The right splanchnic nerves were excised at their entrance into the celiac ganglion, traced above to their exit from the sympathetic chain, then avulsed at that point. Trypsin was determined analytically in the manner described by Hepler[4] and also by the photographic film technic of Kniaskof.[5] Fecal fat was estimated grossly by the use of thin smears stained with scarlet red.

#### REPORT OF CASES

CASE 1.—J. F., a white boy aged 6 years, was referred to Ochsner Foundation Hospital on May 12, 1949 for investigation of bilateral bronchiectasis of the lower lobes of the lungs. Respiratory and nutritive difficulties were first noted in the patient at the age of 2 months and had progressed relentlessly

From the Departments of Surgery (Drs. Ayers and Ochsner) and Pediatrics (Dr. Stowens), Tulane University School of Medicine, and the Ochsner Clinic.

We are indebted to Dr. Otto Schales, Director of Chemical Research, Alton Ochsner Medical Foundation, for his invaluable assistance in the chemical analyses involved in this study.

1. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to the Celiac Disease: Clinical and Pathologic Study, Am. J. Dis. Child. **56**: 344-399 (Aug.) 1938. Blackfan, K. D., and May, C. D.: Inspissation of Secretion, Dilatation of the Ducts and Acini, Atrophy and Fibrosis of the Pancreas in the Infants: Clinical Note, J. Pediat. **13**: 627-634 (Nov.) 1938.

2. Philipsborn, H. F., Jr.; Lawrence, G., and Lewis, K. C.: The Diagnosis of Fibrocystic Disease of the Pancreas, J. Pediat. **25**: 284-298 (Oct.) 1944. Philipsborn, H. F., Jr.; Lawrence, G.; Gibson, S., and Greengard, H.: An Analysis of the Duodenal Drainage in the Steatorrheas, ibid. **26**: 107-119 (Feb.) 1945.

3. Labat, G.: Regional Anaesthesia, ed. 2, Philadelphia, W. B. Saunders Company, 1930.

4. Hepler, O. E.: Manual of Clinical Laboratory Methods, ed. 4, Springfield, Ill., Charles C Thomas, Publisher, 1949.

5. Kniaskof: Med. Klin., 1911, cited by Harrison, G. A.: Chemical Methods in Clinical Medicine, London, J. & A. Churchill Ltd., 1940.

despite almost constant antibiotic therapy. The appearance of a chronic cough, intermittent and prolonged bouts of fever, hemoptysis and night sweats by the time he was 5 years of age had led to bronchographic studies elsewhere, which revealed cylindric dilatation of the bronchi of both lower lobes. Treatment during the next year consisted of postural drainage and the almost constant use of penicillin. An older sister aged 17 years had chronic bronchitis, and one other sibling was well.

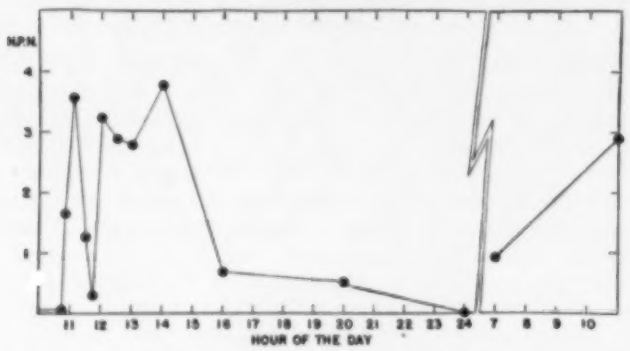


Fig. 1 (case 1).—Tryptic activity per each 100 cc. duodenal fluid expressed in grams of nonprotein nitrogen released from a casein substrate in thirty minutes. Samples taken before and after splanchnic block.

Physical examination disclosed a pale, fairly well developed and well nourished child who appeared to be chronically and seriously ill. He was 44 inches (112 cm.) tall and weighed 43 pounds (19.5 Kg.). Moderate dyspnea at rest, a cough productive of large amounts of tenacious mucopurulent sputum, generalized coarse bronchial rales and occasional scattered showers of moist crepitant rales were present especially at the bases of the lungs. The abdomen was moderately distended, firm and doughy.

Duodenal trypsin assay revealed 0.03 Gm. nitrogen liberated. There was no increase after attempts at stimulation with tenth-normal hydrochloric acid or acetyl beta-methyl choline. Fecal trypsin was identifiable in a 1:1 dilution only. Results of vitamin A tolerance test showed 64, 65, 65 and 65 mg. in fasting 3, 6 and 9 hour specimens, respectively. The serum amylase level was 29 mg. and the serum cholesterol determination was 161 mg., per hundred cubic centimeters.

Hematologic studies, results of urinalysis, blood levels of dextrose, calcium, phosphorus, alkaline phosphatase and urea nitrogen, and results of the dextrose tolerance test were all within normal limits. The electrocardiogram was interpreted

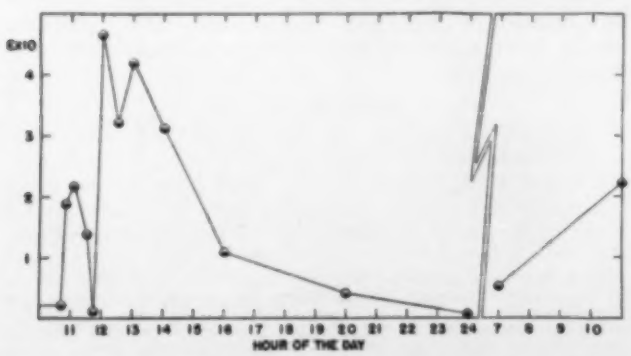


Fig. 2 (case 1).—Tryptic activity per each 100 cc. of duodenal fluid as determined by ultraviolet absorption at 275 millimicrons (meta phosphoric acid filtrate). Samples taken before and after splanchnic block. E × 10 indicates extinction at 275 millimicrons times ten.

as normal. Cytologic studies of the sputum revealed epithelial cells of the squamous type.

Roentgenologic studies of the chest disclosed an increase in bronchovascular markings toward both bases and suggestive evidences of emphysema. There was diffuse clouding of both antral and ethmoidal sinuses. Bronchograms revealed cylindric bronchiectasis of moderate degree in the lower lobes of both lungs, particularly in the medial portions; there was partial atelectasis of the lower lobes as well as bronchiectasis involving the middle lobe and the anterior inferior segment of the upper lobe of the right lung and the posterior medial segment of the lingula. There were only three carpal ossification centers, an indication of skeletal retardation.

On May 14, 1949 a splanchnic block was performed on the right side. A tube had been placed in the duodenum previous to the block and was left there for the next twenty-four hours. Changes in concentration of trypsin in the duodenal contents before and after the block are shown in figures 1 and 2. Simultaneously, the digestive action of the tryptic ferment on the gelatin of a roentgen ray film was determined (fig. 3). Figure 4 shows similar changes in fecal contents before and after the block. As demonstrated by all these investigations, splanchnic block was followed by large increase in trypsin content of the intestinal tract. In addition to the laboratory evidence of increased tryptic activity, there was remarkable symptomatic improvement: the cough became less frequent and productive, breathing was quieter and relatively effortless, the numerous coarse and crepitant rales completely disappeared, and drenching night sweats decreased. These improvements were noted during the first evening, within eight hours after the block. Two days later the stools were firm, formed and brown and had a much less objectionable odor. After removal of the

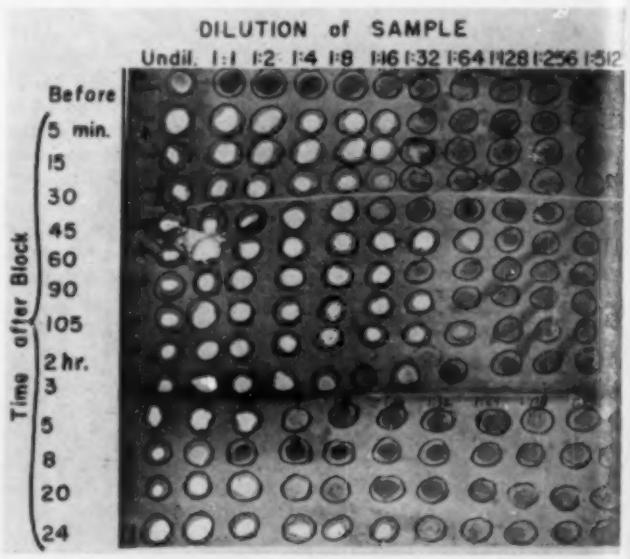


Fig. 3 (case 1).—Photograph of the roentgen ray film test on the preblock and postblock specimens of duodenal fluid. Digestion of the gelatin layer is seen as clearing of the film.

duodenal tube, the clinical course was followed mainly by assays of trypsin in the feces and by physical signs in the chest. In one week the patient's condition had returned to the preblock status, and a complete splanchnicectomy was performed on the right side. The results were essentially the same as those following the preliminary block. Levels of trypsin in the duodenal contents for the next three days are shown in figures 5 and 6. Postoperatively there was a right pneumothorax which was treated by aspiration. Duodenal samples obtained on the sixth postoperative day showed a concentration of trypsin equal to 13.9 Gm. of nitrogen liberated, the highest value we ever obtained from this patient. Beneficial effects were still evident on discharge eight days later.

CASE 2.—G. G. was said to have pneumonia involving all lobes of both lungs at 5 months of age. Foul, bulky, frequent stools were also noted about the same time. She was immediately suspected of having fibrocystic disease of the pancreas because two older siblings had already died of this disease, in 1 instance proved by necropsy; 1 younger sister also has the disease (case 3). Consequently, the infant was treated with the usually prescribed regimen. During the next year she had two more severe infections of the upper part of the respiratory tract, both requiring hospitalization. Her physical growth was slow. When we first saw her at 17 months of age, assay of duodenal material revealed no trypsin. Vitamin A and carotene

were absent from the blood. The previous treatment regimen was continued with the addition of even larger amounts of vitamins A and D. From that time until the present admission she had two more severe respiratory infections and a persistent cough, and noisy rattling respirations continued thereafter.

On admission the infant was 31 inches (78.7 cm.) tall, 27 months of age and weighed 23 pounds (10.4 Kg.); though small, she appeared neither ill nor in distress. Numerous coarse rhonchi and fine rales were heard over the pulmonary fields; the abdomen was protuberant and firm.

Assay of duodenal contents did not reveal trypsin. The feces, which had a foul odor, contained no trypsin but large amounts of free fat. The serum amylase determination was 42 mg. and the serum cholesterol level was 106 mg., per hundred cubic centimeters. Results of a vitamin A tolerance test revealed no vitamin A in any of the specimens. The hemogram, results of urinalysis and levels for blood dextrose, calcium, phosphorus, alkaline phosphatase and chlorides were normal. No abnormalities were noted in a flat plate roentgenogram of the abdomen, and the skeletal age was considered normal.

A splanchnic block performed on the right side the day after admission with the child under local anesthesia proved to be unsatisfactory, so on the following day the procedure was repeated with the patient under vinyl ether anesthesia. Because it was impossible to keep a tube in the duodenum, the course had to be followed by examination of the feces and by observance of the child's clinical appearance. The rhonchi disappeared completely within several hours after the block. After several days the feces became smaller in amount, firmer and of a less foul odor. A transient though slight increase in the amount of trypsin was noted. One week after admission a complete splanchnicectomy was performed on the right side. Again it proved to be impossible to obtain duodenal samples. Splanchnicectomy was followed by decrease in abdominal distention and the appearance of large amounts of bile, unmixed with feces, in the rectum. The appetite and general appearance improved, and although an unrestricted diet was allowed the character of the feces appeared to be essentially normal. Pulmonary signs did not recur. On the first postoperative day gastric ileus and a right pneumothorax of a minimal degree developed but responded to appropriate therapy, and the patient was free from symptoms on discharge eight days later.

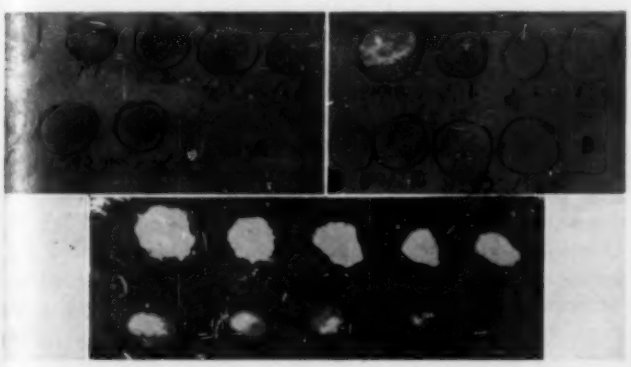

Fig. 4 (case 1).—Photographs of roentgen ray film tests for the tryptic activity of the feces before and after the splanchnic block. Digestion of the gelatin layer is seen as clearing of the film: *A*, May 11, 1949; *B*, May 13, and *C*, May 17.

CASE 3.—M. G. had an attack of pneumonia at 5 months of age, following which foul, bulky and oily stools were noted. Fibrocystic disease of the pancreas was immediately suspected because of its occurrence in three siblings; this diagnosis was confirmed two months later by absence of trypsin in the duodenal contents. Vitamin A was absent from the blood. The patient was treated with the usually prescribed regimen. She had no further respiratory difficulty, but the stools continued to be abnormal in character and her physical development was slow.

On admission May 25, 1949 she was 17 months of age, 27 inches (68.6 cm.) tall and weighed 19 pounds (8.6 Kg.). Her abdomen was extremely protuberant, and there was an unpleasant odor about her. There was no trypsin in the duodenal contents: the feces, which had a foul odor and contained large amounts of fat, also showed no tryptic activity. Results of the vitamin A tolerance test revealed no vitamin A in any of the samples. A roentgenogram of the chest disclosed no abnormalities. The skeletal age was considered normal.

On the day after admission splanchnic block on the right side, attempted with the infant under local anesthesia, was

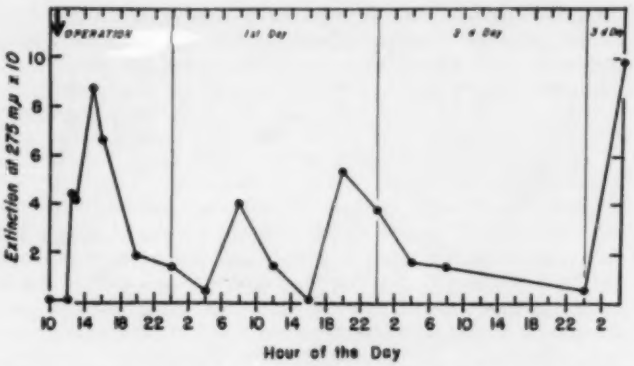


Fig. 5 (case 1).—Tryptic activity per each 100 cc. of duodenal fluid as determined by ultraviolet absorption at 275 microns (meta phosphoric acid filtrate) of the samples collected immediately prior to and for sixty-seven hours after right splanchnicectomy.

unsatisfactory because of poor cooperation, so it was repeated the following day with the infant under vinyl ether anesthesia. Eight cubic centimeters of a 1 per cent solution of procaine hydrochloride was injected. It was not possible to keep a tube in the duodenum, and the course had to be followed by the clinical signs and alterations in the stools. Improvement in gastrointestinal tone and motility was evidenced by reduction of abdominal distention and appearance in the rectum of a large amount of bile unmixed with feces. The feces changed from formless, bulky, malodorous, fatty material to fairly firm, formed specimens which, although containing only minimal

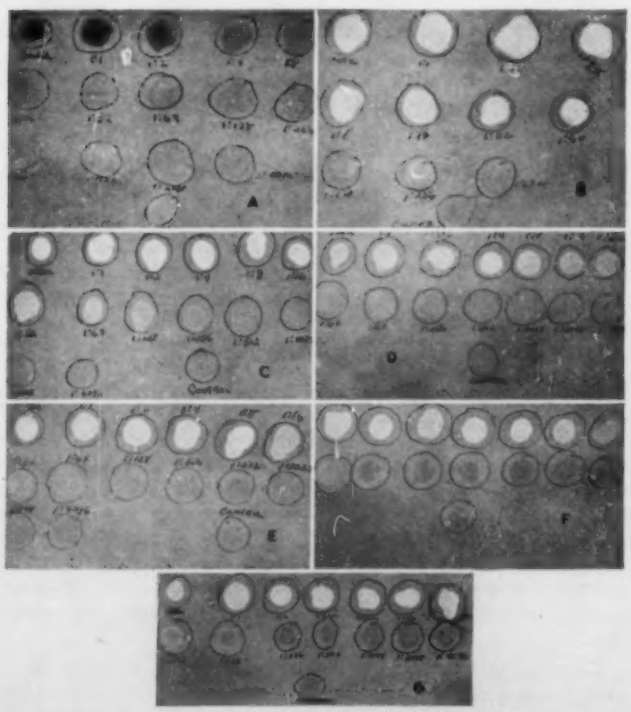

Fig. 6 (case 1).—Roentgen ray film tests for tryptic activity of the duodenal fluid collected before and at various times after splanchnicectomy. Digestion of the gelatin layer is seen as clearing of the film. *A*, preoperative, May 23, 1949, 8 a. m.; *B*, postoperative, May 23, 12:30 m.; *C*, May 23, 3 p. m., five and one-fourth hours postoperative; *D*, May 23, 8 p. m., ten and one-fourth hours postoperative; *E*, May 24, 8 a. m.; *F*, May 25, 8 a. m.; *G*, May 29, six days postoperative, 10:15 to 11:45 specimen.

traces of trypsin, were considerably less offensive in odor and contained much smaller amounts of fat. Similar clinical improvement followed complete splanchnicectomy on the right side performed on June 1. Again it proved impossible to obtain duodenal material for assay. Postoperatively, despite an unrestricted diet, she had only one to two fairly normal bowel movements daily instead of the five to seven prior to operation. She was completely free of symptoms on discharge from the hospital eight days after operation.

CASE 4.—M. A. had a respiratory complaint diagnosed as asthma at four months. Prior to this he had had rather persistent colic, for which he was not treated specifically. At seven months six to seven bowel movements were noted daily and the feces were fatty, bulky and foul smelling. Respiratory difficulties continued, and by the time the child was one year of age they had taken the form of a paroxysmal cough. The abdomen had become extremely protuberant. The child was unusually small, and physical development was slow. He did not walk until 17 months of age. At 18 months of age he was given pancreatic extract, although no diagnostic procedures had been performed. At this time severe pneumonia developed, following which the respiratory symptoms became severer. By the age of 2 years a chronic cough, constant, low grade fever and night sweats had appeared. The diagnosis of fibrocystic disease of the pancreas was established at the age of 2½ years by assay of duodenal contents for trypsin. Despite the institution of the usual therapeutic regimen his condition rapidly became worse, especially the respiratory symptoms.

On admission at the age of 3½ years, the child was 35 inches (88.9 cm.) tall, weighed 27 pounds (12.2 Kg.) and appeared seriously but chronically ill. Moderate dyspnea was apparent even at rest, and he was able to leave his bed only for short periods. He had a frequent paroxysmal cough productive of a thick viscid mucoid sputum. There was diminution in breath sounds in all pulmonary fields, and the chest appeared emphysematous; no rales were heard. Pulmonary osteoarthropathy was present in all four extremities. There was a moderate degree of exophthalmus.

Assay of duodenal contents revealed no trypsin. The feces contained no trypsin and small amounts of fat. The vitamin A blood level was 29 mg. per hundred cubic centimeters. The serum amylase level was 7 mg. and the serum cholesterol level 70 mg., per hundred cubic centimeters. The hemogram, results of urinalysis, and blood determinations of dextrose, phosphorus, calcium and alkaline phosphatase were within essentially normal range.

A roentgenogram of the chest showed increased bronchovascular markings about the hilum extending well into the middle of the pulmonary fields. Bone maturation indicated skeletal retardation, and some osteoporosis was present. On June 7 following splanchnic block on the right side with 10 cc. of a 1 per cent solution of procaine hydrochloride, with the child under vinyl ether anesthesia, dyspnea was somewhat relieved and the cough became less frequent, less severe and productive of smaller amounts of sputum of a thinner consistency than previously. Abdominal distention was greatly reduced, and the gastrointestinal motility and tone were visibly improved. Samples of the duodenal contents, however, showed no increase in the concentration of trypsin. Following the block the child had moderate fever and a rapid pulse for two days but was otherwise greatly improved. On June 11 during splanchnicectomy cardiac arrest occurred, and despite prolonged cardiac massage and other resuscitative measures the patient died.

CASE 5.—C. H. began to have large, pale, frequent bowel movements while he was still in the nursery for newborn infants. During his first year of life he was hospitalized three times because of attacks of pneumonia. Despite the usual therapeutic regimen the respiratory symptoms gradually progressed. A diagnosis of fibrocystic disease of the pancreas by absence of trypsin in duodenal contents was first made when the patient was 1 year of age.

On admission June 1, 1949 the patient, who was 2 years of age, 32 inches (81 cm.) tall and weighed 26 pounds (11.8 Kg.), was pale and did not seem to be vigorous. Except for a frequent cough productive of moderate amounts of thick, tenacious, mucoid sputum he did not appear seriously ill. The lungs were filled with coarse rhonchi, and occasional rales could be heard. The abdomen was moderately distended.

No trypsin could be demonstrated in the duodenal contents. The feces, which had a foul odor, contained no trypsin but moderate amounts of fat. Determination of serum amylase was 43 mg. and serum cholesterol 97 mg., per hundred cubic centimeters. The blood vitamin A level was 68 international units per hundred cubic centimeters.

On the day after admission, with the child under vinyl ether anesthesia, splanchnic block was performed on the right side with 10 cc. of a 1 per cent solution of procaine hydrochloride. Because insertion of a duodenal tube caused almost continuous vomiting, duodenal samples could not be collected. Following block the cough was nonproductive and decreased in frequency and severity. The rhonchi and rales were no longer heard. The stools decreased from three to five daily to one to three daily and lost their foul odor. No fat was visible in the feces. However, there was no increase in the amount of trypsin. The patient remained well for ten days, after which the respiratory signs gradually began to reappear. Eleven days after the block complete splanchnicectomy was performed on the right side. The respiratory signs immediately disappeared, and the other changes observed after the block were again noted. The patient was discharged from the hospital on the seventh postoperative day after an uneventful postoperative course.

### THEORY OF NEUROEFFECTOR MECHANISM

That improvement in the digestive manifestations in these cases may have resulted from an increase in local blood supply to the pancreas is indicated by the increase in its exocrine secretions noted in case 1. Previously the respiratory lesions in fibrocystic disease were thought to be due to deficiencies, probably of vitamin and other substances caused by altered intestinal absorption secondary to absence of pancreatic ferments. The dramatic changes in the respiratory symptoms cannot be explained on the basis of increased pancreatic vascularity, however, because their appearance seemed too prompt to allow such a conjecture. We believe that the rapidity of improvement in the pulmonary symptoms limits a satisfactory explanation of the mechanisms of some changes in the nervous system. Our present concept concerning these mechanisms is as follows: The diseased pancreas acts as a source of afferent impulses of abnormal degree to the spinal and diencephalic centers. The syncytial nature of the reticular substance in the spinal cord and the diencephalon allows diffuse dissemination of efferent impulses therein with facilitation by bulbar facilitatory mechanisms as has been demonstrated experimentally. There follows, then, a diffuse discharge of efferent stimuli to all viscera.[6] Assuming the existence of such a mechanism, one can see how a pancreatic disease can produce pulmonary or gastrointestinal manifestations. It is believed, therefore, that when the pancreas in fibrocystic disease is denervated, an abnormally functioning reflex arc is interrupted, reestablishing a normal level of autonomic activity to those organs adversely affected through their reflex connections in the spinal cord and diencephalon with the pancreas.

The following facts are further suggestive evidence of such relationships. 1. The pancreas and lungs arise from the same portion of the embryologic midgut. 2. The lungs, pancreas and gastrointestinal tract have a common efferent nervous pathway in the vagus nerve. (Although the sympathetic supply to these structures has its gross anatomic outflow from different levels,

6. Bach, L. M. N.: The Role of the Bulbar Facilitatory and Inhibitory Systems in Vasomotor and Respiratory Activity, Federation Proc. 7: 4 (no. 1, pt. 1) (March) 1948.

the numerous and complete interconnections between all parts of this system with any other part within the spinal cord and diencephalon make it possible to view the autonomic system as an anatomic and functional entity.) 3. There are numerous references in the experimental literature to substantiate the existence of reflex arcs similar to that hypothesized here.[7] 4. That respiratory or otitic infections are frequently associated with gastrointestinal symptoms is an old pediatric observation. 5. It has long been noted by internists that there is a close association between cholecystitis and cardiac disease.[1] 6. Adynamic ileus not infrequently follows numerous insults affecting apparently unrelated viscera, such as pneumonia, acute renal failure and fractures. Many similar "peculiar" associations might be cited. 7. Experimental evidence of reflex bronchospasm, increased bronchial secretions and reflex cardiac effects following stimulation of abdominal viscera has been widely accepted.[7a] Figure 7 is a schematic representation of the reflex nervous pathways.

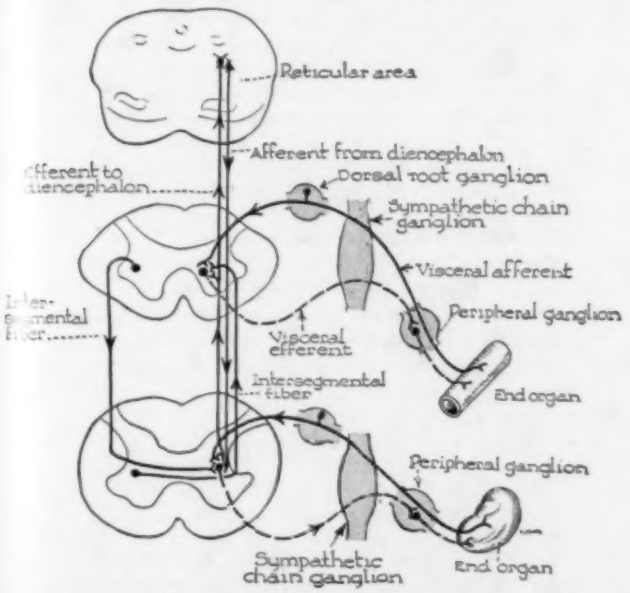


Fig. 7.—Schematic representation of autonomic interrelationships within the spinal cord and diencephalon.

## COMMENT

The implications which may be drawn from such a hypothesis are too numerous to be considered here except as they relate to the present problem. We believe that an approach based on this concept of related symptomatology in fibrocystic disease of the pancreas should justify splanchnicectomy whether or not any specific evidence of an increase in pancreatic exocrine function is obtained by means of procaine block. This opinion is based on the belief that the poor nutritive function in these children is not caused solely by the poor exocrine function of the pancreas but is also influenced by the reflexly produced poor function of the gastrointestinal tract as a whole. The reflexly produced respiratory signs and symptoms are also greatly benefited. That the functions of these two systems are improved by this procedure has been shown by the cases reported. The gradations of response in the increase in the amount of trypsin in the various patients are probably explainable on the basis of variations of the amount of glandular tissue spared by the disease.

The occurrence of 1 surgical death in this small series is indicative of the fact that the operation is not without danger, though such a risk appears to be justifiable in this otherwise uniformly fatal disease. One death in 5 cases compared with the alternative eventual 100 per cent case mortality rate does not make even this high value seem prohibitive. Observations on the patient who died also support theories we have expressed as to mechanisms underlying the beneficial effects achieved, for after complete necropsy the cardiac arrest was considered to be on a reflex basis. This death emphasized the importance of the use of adequate doses of atropine preoperatively. A preoperative splanchnic block appears to reduce the bronchial secretions effectively. This greatly simplifies the induction of anesthesia and also tends to ameliorate the inspissating effects of atropine on the bronchial secretions. It has also seemed advisable to instill several cubic centimeters of procaine about the celiac ganglion prior to manipulation of the splanchnic nerves themselves at operation. In the 1 patient operated on after the fatality, it was noted that when the celiac ganglion was injected with procaine in an attempt to avoid possible adverse cardiosplanchnic effects, the heart dropped several beats.

Analysis of the duodenal contents for enzymic activity is the one absolute means of establishing the diagnosis. However, in extremely young patients the combination of passing a large enough tube through the nose, inserting it into the duodenum and keeping it there results in complete physical exhaustion, especially in these patients already debilitated by the disease. In 1 patient this procedure caused such exhaustion that it was deemed necessary to postpone operation for this reason. Analysis for trypsin by the photographic film technic already referred to has shown that a close correlation exists between the amount of trypsin in the duodenal contents and feces. Consequently, because of the trauma coincident with duodenal intubation, the simpler technic of fecal analysis is considered more desirable and sufficiently accurate to follow the course of the disease once the diagnosis has been established. It is to be emphasized, however, that trypsin content and character of the feces should not be used as the only guide to success of the treatment. The general physical improvement of the patients, especially in regard to pulmonary and gastrointestinal symptoms, far outweighs any specific alteration in the amount of trypsin which appears in the gastrointestinal tract.

The use of the vitamin A tolerance test, although valuable as confirmatory evidence of the diagnosis, has been found to be a difficult analysis to obtain in this area; it is generally not completely reliable and is extremely expensive. These factors have precluded its routine use.

## CONCLUSIONS

This preliminary report is considered justifiable because a new concept of treatment of fibrocystic disease of the pancreas, consisting of sympathetic denervation of the pancreas by splanchnic block with procaine hydrochloride and complete splanchnicectomy on the right side, has been evolved. This treatment, even in

7. (a) DeTakats, G.; Fenn, G. K., and Jenkinson, E. L.: Reflex Pulmonary Atelectasis, J. A. M. A. **120**: 686-690 (Oct. 31) 1942. (b) Burstein, C. L., and Rovenstine, E. A.: The Reflex Complicating Anesthesia During Abdominal Surgery, Anesth. & Analg. **17**: 134-143 (May-June) 1938. Kuntz, A., and Haselwood, L. A.: Cutaneo-Visceral Vasomotor Reflexes in the Cat, Proc. Soc. Exper. Biol. & Med. **43**: 517-519 (March) 1940. Gilbert, N. C.; Fenn, G. K., and LeRoy, G. V.: The Effect of the Distention of the Abdominal Viscera on Coronary Blood Flow and Angina Pectoris, J. A. M. A. **115**: 1962-1967 (Dec. 7) 1940. Bach.[6] These references were supplied by Dr. L. M. N. Bach, head of the Department of Neurophysiology, Tulane University of Louisiana School of Medicine.

its early stages, shows promise of limiting the secondary and fatal complications of the disease. In addition, the evidence indicates that disease of one viscus can be responsible for functional changes in other viscera. These secondary functional changes finally produce pathologic alterations in the affected viscera characteristic of primary disease of those (the affected) organs; that is, the bronchiectasis seen in fibrocystic disease is the same pathologically as the bronchiectasis following, for example, primary pneumonia. It is also indicated that these phenomena are mediated through a neuro-effector mechanism by the establishment of abnormal reflex arcs and that physical interruption of such an arc can have beneficial effects on the reflexly involved organs.

## COMPLICATIONS WITH THE USE OF A PARASYMPATHETIC-STIMULATING DRUG

### Development of Acute Pyelonephritis in Neurogenic Bladder

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The parasympathetic-stimulating drugs are important adjuncts in the treatment of atonic and hypotonic bladders. The clinical toxicity, precautions and contraindications in their use have been well documented.[1] During the use of one of these drugs, furmethide® (furfuryl trimethylammonium iodide),[2] in the cases to be cited from the practice of one of us (C. N.), a complication developed which, to our knowledge, has not been previously reported. Acute pyelonephritis developed during effective therapeutic dosage of furmethide® in 2 patients, both of whom had a large amount of residual urine and vesicoureteral reflux.

#### REPORT OF CASES

CASE 1.—S. J., a 3 year old white girl, was first observed on Sept. 23, 1946. The child had been delivered at the eighth month of gestation, weighing 5 pounds 7 ounces (2,466 Gm.). The obstetrician noted that the infant had a spina bifida with meningocele. When she was 3 weeks of age the meningomyelocele at the fifth lumbar segment was repaired. The child then developed satisfactorily except for urinary and bowel difficulties. The urine was always infected. She had repeated attacks of chills and fever until she was 2 years of age. The parents believed that the child had a sensation of bladder fulness, but she was unable to control urination and dribbled urine almost continuously, day and night. The child had always been severely constipated, requiring several enemas weekly, with incontinence when she had semisoft stools. The family history was noncontributory.

The patient was found to be a thin, chronically ill child of 3 years, who walked normally. The bladder was felt 3 fingerbreadths above the symphysis pubis, and there was moderate loss of rectal sphincter tone, with dilatation of the rectum above. Neurologically, there was slight diminution of pinprick and cotton touch appreciation perianally. The left ankle jerk was slightly greater than the right. There were no abnormal reflexes. A healed operative scar was present over the lower lumbar region of the spine and the sacrum.

Tests of the blood revealed 70 per cent hemoglobin. Tests of the urine showed: specific gravity, 1.012; $p_H$, 7.5; albumin, 1 plus; sugar, negative; 25 to 30 white blood cells and 3 to 8 red blood cells per high power field. Cultures showed Bacillus coli, Bacillus subtilus and Enterococcus. A cystometric reading revealed an atonic bladder with no voiding reflex. There was 295 cc. of residual urine; the capacity of the bladder was 625 cc. An intravenous pyelogram showed no calculi; the right kidney was normal in size, shape and position, and the calices and pelvis were normal. The left kidney was not clearly visualized, but there was faint excretion of the dye. A no. 13 McCarthy baby cystoscope was passed with ease. Cystoscopic examination disclosed that the bladder was mildly inflamed and trabeculated; there were no tumors, diverticula or calculi. Both ureteral orifices were mildly gaping. The internal sphincter moved slightly on voiding attempts. A large funnel urethra extended nearly to the external meatus. A cystourethrogram (fig. 1) revealed also a huge oval-shaped bladder, tilted slightly to the right. There was bilateral vesicoureteral reflux, which revealed bilateral hydroureters and hydronephrosis.

*Course.*—The mother was advised to keep the child on a normal fluid intake and encourage her to void every three hours.

On Nov. 17, 1946 the patient was given furmethide,® 2.5 mg. subcutaneously every eight hours and 5 mg. orally one and a half hours after each injection for three days. She was then given the drug orally, 5 mg. four times a day.

On November 20 her temperature rose to 103 F., and she had pain in the right lower part of the abdomen radiating to the right flank. The urine showed numerous pus cells and albumin (1 to 2 plus). On November 23 the amount of residual urine was 75 cc. She was given sulfathiazole, 1 Gm. three times a day, and penicillin, 20,000 units intramuscularly five times a day, for three days. Her temperature returned to normal, and the urine cleared remarkably. There was no albumin and only 2 to 3 white blood cells per high power field.

On November 29 the administration of furmethide® was discontinued because the temperature again rose to 103 F. The patient was again given the therapy previously mentioned.

By November 30 the amount of residual urine was 312 cc. The administration of sulfathiazole was now discontinued, but penicillin was given until December 4. She was catheterized intermittently during the day beginning December 1. Sulfathiazole was given from December 5 to December 8. On December 7 furmethide® was given as before. The amount of residual urine, which was 125 cc. on December 9, fell to 40 cc. by December 19. Because of the high content of pus in the urine, oral administration of penicillin, one 50,000 unit tablet every three hours, was begun on December 9 and continued until December 13, during which time the pus count dropped. The temperature hovered near 100 F. at night, with continued slight abdominal pain which had begun on December 10. By December 19 the temperature had risen to 103 F. and the urine was full of pus cells; the albumin reaction was 1 to 2 plus. The abdominal pain had become severe. The pain was similar to that previously described, beginning in the right lower quadrant and radiating into the back. Pain was relieved the next day when the administration of furmethide® was stopped. Ammonium mandelate, 4 tablets (0.5 Gm.) three times a day was given as well as penicillin until December 30, during which time the temperature fell to 99 F. at night. However, the amount of residual urine had increased to 220 cc. by December 22.

Because of the increasing amount of residual urine, furmethide® was given for the third time, on Jan. 3, 1947, 2.5 mg. orally four times a day. However, since the child again experienced similar abdominal pain and had a temperature of 102 F., administration of the drug was stopped the next day. The urine, as on each previous episode, contained a large number of pus cells and showed albumin (1 to 2 plus).

On January 19 a Malecot 14F catheter was left indwelling in the bladder. This remained until May 2, when a suprapubic cystostomy was performed because of a urethritis; a no. 28 Pezzar tube was used. During the previous four month period with the indwelling catheter, the patient had remained afrebrile, without pain and with clear urine. Urea nitrogen of the blood was 11.1 mg. per hundred cubic centimeters on May 1.

After the cystostomy the patient had occasional fever with many pus cells in the urine when there was not proper drainage through the tube. She gained weight and progressed well.

1. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941, pp. 363-364.
2. Lipton, J. H.; Beaser, S. B., and Altschule, M. D.: Action of Furmethide (Furfuryl-Trimethyl-Ammonium Iodide) on Bladder in Patients with Urinary Retention Following Surgery on Rectum: Preliminary Report, New England J. Med. **226**:138 (Jan. 22) 1942. Beaser, S. H.; Lipton, J. H., and Altschule, M. D.: Further Experience with Furfuryl-Trimethyl-Ammonium Iodide (Furmethide) in the Treatment of Urinary Retention Due to Bladder Atony, Am. J. M. Sc. **206**:490 (Oct.) 1943.

In August 1948 furmethide® was again prescribed, when it was found that the child could not empty her bladder after the tube was clamped. The drug, 5 mg. orally four times a day, was given for three days. The amount of residual urine dropped from 100 cc. to 40 cc., and there was no febrile reaction or pain as was previously experienced. It is to be noted that except during tests for residual urine there was free drainage through the tube. Administration of furmethide® was discontinued, not because of any untoward reaction but because it was thought best to continue the suprapubic drainage without attempts to remove the tube with any other procedure.

CASE 2.—R. D. L., a 28 year old white man, was first seen on Aug. 12, 1946. Past history revealed that he had had pneumonia at the ages of 3, 10 and 15 years and an appendectomy at age 24. His present illness had begun in 1943 with an attack of what was diagnosed as influenza; at that time he had an infection of the upper part of the respiratory tract accompanied with general malaise. Three weeks after the onset he had severe intermittent nonradiating pain in the lower thoracic and lumbar region of the back, associated with fever, cough and whitish phlegm. His feet became cold, and he could not void. He was taken to a hospital for catheterization and was discharged the same day. On leaving the hospital, he noted definite weakness of the legs. The following day he was unable to move his legs. He was again hospitalized on Dec. 18, 1943. He was found to have anesthesia and loss of motor power from the level of the fourth thoracic segment on the left and the fifth thoracic segment on the right, with slight nuchal rigidity. Lumbar puncture revealed clear fluid under normal pressure, no block on jugular compression, normal sugar content, slightly increased globulin content and 400 lymphocytes per cubic millimeter.

Three days later a repeat lumbar puncture showed slightly yellow fluid, normal sugar content and 100 lymphocytes per cubic millimeter. The temperature remained at 101 F. Iodized oil instilled into the spinal canal revealed no block. The paralysis remained the same. Another puncture, one week later, revealed decidedly xanthochromic fluid under normal pressure, no block, increased globulin content and no cells. The next day, at laminectomy, from the fifth to the eighth thoracic segments, no block was found, even with a long probe extended in both directions; the dura was opened, and the cord appeared dull and lusterless. The postoperative diagnosis was transverse myelitis with destruction of the cord.

Since that time the patient has shown no signs of improvement. There was complete loss of erection and nocturnal emission. He had no control of bowel movements and no feeling of fulness in the rectum; he required enemas every three days. He had no control of urination, and leaking was almost continual. There were vague sensations of fulness in the bladder, but the patient had no ability to start or stop the stream.

Six months after leaving the hospital he had an attack of chills and fever. On hospitalization he was found to have urinary tract infection, and tidal drainage was instituted. He was advised to use an indwelling urethral catheter and to have this changed once weekly. He had continued on this regimen for two years prior to the present examination.

When the patient came under the care of one of us (C. N.), on Aug. 12, 1946, there was a complete flaccid paraplegia with a sensory level at the fifth thoracic segment on the right and the fourth thoracic segment on the left, complete areflexia below this level and no motor power. There was a large decubitus ulcer 2 inches (5 cm.) in diameter over the right ischial tuberosity. There was almost complete loss of anal sphincter tone. A healed laminectomy scar extended from the sixth to the tenth thoracic segment. Blood pressure was 105 systolic and 70 diastolic. The right kidney was palpable. The liver was just palpable at the costal margin. A no. 18 indwelling Foley urethral catheter was in place.

The $p_H$ of the urine was 7.5, specific gravity, 1.020, with no albumin or sugar. There were occasional white blood cells but no red blood cells or casts. Methylene blue smear showed rods. Culture revealed Bacillus proteus. An intravenous pyelogram made on August 16 disclosed four large calculi in the bladder. There was prompt excretion of dye bilaterally, and the pelvis and calices of the left kidney were normal. There was slight dilatation of the lower end of the left ureter. On the right, the calices and pelvis were slightly dilated but essentially normal; the lower two thirds of the ureter was slightly dilated. Cystoscopic examination was made on September 23. A no. 24 panendoscope was passed with ease. The internal sphincter was moderately dilated and did not move on voiding attempts. There was a funnel-shaped posterior urethra with pseudosphincter formation.[3] The external sphincter was moderately dilated and did not move on voiding attempts. There were four large, hard, grayish white calculi in the bladder, varying in diameter from 2 to 5 cm. The bladder was severely inflamed and edematous. A cystometric reading on August 14 had shown greatly increased bladder pressure without a voiding reflex. Fluid leaked around the catheter after 75 cc. had run in. A cystogram made on September 2 (fig. 2) revealed that the bladder was slightly larger than normal and leaned to the right. There was right vesicoureteral reflux with a large funnel urethra. Four calculi could be seen in the bladder. There was some dilatation in the region of the external sphincter. The reflux showed that

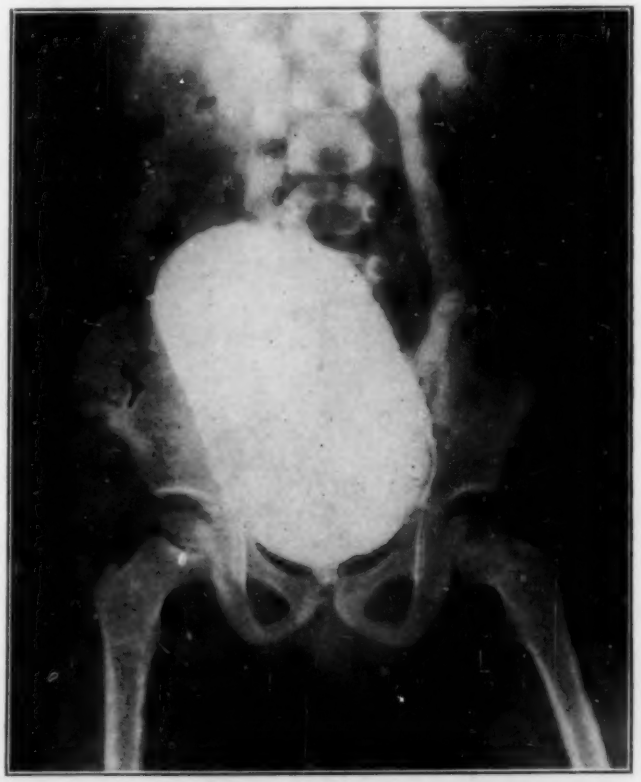

Fig. 1 (case 1).—Atonic bladder showing bilateral vesicoureteral reflux and a funnel urethra.

there was a dilatation of the right ureter with a moderate hydronephrosis.

Cystolithotomy was performed at Montefiore Hospital on September 3. Four calculi were removed from the bladder; one was 2 inches (5 cm.) in diameter, and the others were 1 inch (2.5 cm.) in diameter. A suprapubic tube was left in the bladder. Chemical analysis of the calculi showed calcium carbonate, calcium phosphate and a small amount of ammonium magnesium phosphate. Urea nitrogen in the blood was 9.9 mg. per hundred cubic centimeters. Tests of the blood showed: 93 mg. sugar per hundred cubic centimeters, 10 Gm. hemoglobin, 3,300,000 red blood cells, 11,700 white blood cells, 74 per cent polymorphonuclear cells, 2 per cent juvenile forms, 17 per cent lymphocytes, 2 per cent eosinophils and 5 per cent monocytes. Reactions to Wassermann and Kahn tests were negative. While the patient was in the hospital a large decubitus ulcer developed over the sacrum.

On September 21 the suprapubic tube was removed and a catheter was put into the urethra. On October 19 the patient, seen at the office, had a temperature of 103 F. and decidedly

3. Ney, C.; Auerbach, O., and Hoen, T. I.: Pseudo-Sphincter Formation in Neurogenic Bladder, J. Urol. 57: 858 (May) 1947.

purulent urethritis. The catheter was removed, and he was given sulfathiazole, 1 Gm. four times a day for one week. He became afebrile. The urine then contained 5 to 6 white blood cells per high power field with a few clumps. The ulcer of the sacrum had improved.

On November 29 a cystometric reading revealed a hypotonic bladder with a capacity of 500 to 600 cc., residual urine of 400 cc. and no voiding reflex.

On December 14 a cystoscopic examination was made; a no. 24 panendoscope was passed with ease. The bladder was of large capacity and slightly inflamed; there were no calculi, diverticula or tumors. The internal sphincter was fairly well developed but moderately relaxed. It moved paradoxically on voiding attempts, that is, the posterior lip moved upward instead of downward. There was questionable movement of the external sphincter.

On December 30 another cystoscopic examination gave similar findings. It was felt that the main obstruction in the urethra was at the pseudosphincter.

Fig. 2 (case 2).—Hypotonic bladder showing right-sided vesicoureteral reflux and a funnel urethra.

On Jan. 1, 1947 a cystourethrogram was made: an irregular bladder with some elongation in the anteroposterior diameter was found. There was right vesicoureteral reflux. There was a funnel urethra with some narrowing at the distal prostatic portion. The external sphincter appeared dilated. A post-voiding roentgenogram showed that the dye escaped through the internal sphincter but was stopped at the pseudosphincter.

On February 10 the patient was given furmethide,® an injection of 1 ampul (5 mg.) every eight hours and 10 mg. orally one and a half hours after each injection.

On February 14 the patient had a high temperature, 103 to 104 F., with chills. He had a feeling of tenseness over the right kidney. The urine contained albumin (1 plus) and many white blood cells. He was given sulfathiazole, 1 Gm. three times a day for five days.

On February 15 administration of furmethide® was stopped. The temperature rapidly returned to normal, and the feeling of tenseness over the right kidney disappeared, but the urine still contained albumin (1 plus) and 8 to 10 white blood cells per high power field. The amount of residual urine had dropped to 100 cc.

After the administration of furmethide® was stopped, the amount of residual urine gradually mounted to 300 to 400 cc.

On April 23 the patient was admitted to Beth David Hospital. The next day a transurethral resection of the internal sphincter and a partial resection of the pseudosphincter were performed. Urea nitrogen in the blood was 20 mg. per hundred cubic centimeters; creatinine, 1.5 mg. per hundred cubic centimeters; blood sugar, 86 mg. per hundred cubic centimeters; hemoglobin, 80 per cent; red blood cells, 3,900,000, and white blood cells, 8,950, with a normal differential count. There was considerable postoperative bleeding, and a transfusion of 500 cc. of citrated blood was given.

On April 25 he was given penicillin, 30,000 units intramuscularly every three hours. Next day the catheter was removed. On April 28 the amount of residual urine was 100 cc. The patient was discharged on April 29.

On May 9 he was again seen at the office. His residual urine was 475 cc. During this interval he had had difficulty in voiding and was unable to empty his bladder completely, even with severe straining.

On May 26 he had a moderate hemorrhage through the urethra; he was hospitalized near his home for twenty-four hours. The bladder was lavaged and the bleeding easily controlled. The patient was advised to reenter the hospital for another transurethral resection, since the amount of the residual urine averaged 275 cc. This he refused to do, and, on his own, he kept an indwelling catheter in the urethra during the day and removed it at night.

On November 23 an intravenous pyelogram showed no calculi. There was prompt excretion of the dye bilaterally. The pelvis and calices of the left kidney and the upper part of the ureter were normal. The lower third of the ureter was slightly dilated. On the right there was slight dilatation of the pelvis and calices; the ureter was not distinctly seen.

During the succeeding year, except for an occasional attack of fever accompanied with cloudy urine, the patient fared remarkably well. He gained weight; his bed sores were almost healed, with the exception of the draining decubitus ulcer over the right ischial tuberosity. He was able to get about on his crutches and braces.

On Aug. 27, 1948 an intravenous pyelogram revealed no calculi. There was prompt excretion of the dye bilaterally; the ureters on both sides were not distinctly seen, but the pelvis and calices were normal bilaterally.

The patient continued to get along well, gained weight and was up and about on his crutches.

On May 15, 1949 an intravenous pyelogram revealed no calculi; there was prompt excretion of the dye bilaterally; the pelvis and calices were normal bilaterally. There was slight dilatation of the lowermost portion of both ureters. The patient had continued his practice of using the indwelling catheter in the daytime. Cystoscopic examination on this date revealed that the bladder was moderately inflamed; there were no calculi, diverticula or tumors. The funnel urethra and the well developed pseudosphincter could still be seen. Cystometric reading revealed mild hypotonicity of the bladder.

## COMMENT

Furmethide®, a parasympathetic stimulant, was administered to 2 patients with neurogenic bladders, one atonic and the other hypotonic. In both instances an effective parasympathetic response, sweating, salivation and contraction of the bladder, was obtained.

Both patients had a large amount of residual urine and vesicoureteral reflux, bilateral in case 1 and right-sided in case 2.

During furmethide® therapy there was fever and an increase of albumin and pus cells in the urine. In case 1, in which sensation in the abdominal area was intact, actual pain occurred in the right lower quadrant, radiating to the back. In case 2, in which there was complete anesthesia below the fifth thoracic segment, a feeling of tenseness was experienced in the right lumbar area. In both patients almost immediate improvement supervened on discontinuance of the drug.

It is our contention that the effective bladder contractions produced by the furmethide® forced (under greater pressure than had previously existed) urine up the ureter into the kidney, causing acute pyelonephritis. It may be assumed that the resistance to the outflow of urine from the bladder through the urethra was greater than the resistance to the reflux up the ureter. Actually, in case 1, the urethral resistance was by-passed at a later date by a functioning suprapubic tube, after which the administration of furmethide® did not cause acute pyelonephritis.

### SUMMARY AND CONCLUSIONS

The administration of furmethide® (furfuryl trimethylammonium iodide), a parasympathetic-stimulating drug, to 2 patients with large amounts of residual urine and vesicoureteral reflux produced acute pyelonephritis. The pyelonephritis was caused, in our opinion, by the backflow of urine up the ureter into the kidney from a bladder forcibly contracting against a urethral resistance greater than the reflux resistance. In case 1 administration of the same drug after the introduction of a functioning suprapubic tube failed to produce pyelonephritis.

The use of any parasympathetic-stimulating drug in the presence of a large amount of residual urine and vesicoureteral reflux is contraindicated. This report is not to be construed as a condemnation of the particular drug, furmethide®, as we believe that any effective parasympathetic-stimulating drug would produce the same complication.

745 Fifth Avenue (22).—2661 Decatur Avenue (58).

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## STELLATE GANGLION BLOCK IN THE TREATMENT OF ACUTE CEREBRAL THROMBOSIS AND EMBOLISM

### Report of Forty-Four Cases

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The treatment of cerebral thrombosis and embolism is usually unsatisfactory and until recently has been confined to the use of general measures. A patient with thrombosis is often given intravenous fluid, whisky or nicotinic acid and symptomatic treatment. However, the benefit to the patient from this type of treatment does not seem great. In regard to embolism the author of one textbook on neurology says, "Treatment of embolism is discouraging indeed. There is little that can be done. . . ." [1] Renewed interest in the problem of effective therapy has been stimulated by the publication of a number of reports that cite improvement in the clinical status of patients with cerebral thrombosis or embolism treated with stellate ganglion block.

In a paper published in 1946 Risteen and Volpitto [2] claimed favorable results with such treatment. Further attention was drawn to this subject by the publication in 1948 of the study of Gilbert and deTakats,[3] who found that considerable objective improvement often occurred within an hour after the stellate ganglion ipsilateral to the cerebral lesion was blocked. These and other reports are evidence that effective treatment begun a few hours after the onset of cerebral thrombosis or embolism will increase the likelihood of a patient's recovery or at least reduce the degree of his disability. The pathologic process at work in those patients who improve must be reversible, as it is a well known fact that those portions of the central nervous system that are destroyed do not regenerate. Therefore, the neurologic disorders that disappear after treatment or, as occasionally happens, spontaneously improve are present as a result of transient changes rather than destruction of nervous tissue.

Thrombosis and embolism produce local anoxia by interfering with the regional blood supply. It is thought that vasospasm and perhaps vasodilatation are to a degree responsible both for the reversible phenomena and for the spread of the pathologic process.[4] Treatment that restores or increases the circulation in the ischemic areas should cause a return of the function of nervous elements not irreversibly damaged and should prevent the development of further injury. The extreme sensitivity of the brain to anoxia makes early treatment essential.

In a series of remarkable experiments Villaret and Cachera [5] produced artificial cerebral embolism in dogs and watched the pial vessels through windows in the skull. Photographs demonstrated the occurrence of a decided spasm of the vessels in the pia. This spasm was present even in areas not directly affected by the embolus and persisted at times for weeks. Later studies revealed that cerebral infarcts had occurred. It was clearly shown that the noxious local stimulus of the embolus was spread by some means to other parts of the same vessel.

The cerebral vessels are supplied with both sympathetic and parasympathetic nerves, the former from the carotid plexus and the latter from the geniculate ganglion.[6] The sympathetic supply is through the roots of the upper thoracic segments of the spinal cord and is carried upward to the carotid plexus by way of the stellate and cervical ganglions. Blocking or stimulating the nerve fibers at any point along this route would affect the impulses passing to the perivascular sympathetic nerves and presumably by this means would alter the cerebral blood flow.

In 1837 Bracht sectioned the cervical sympathetic nerve and found that cerebral congestion ensued.[7] Van der Becke Callenfelds demonstrated in 1855 that excitation of the same nerves caused contraction of the cerebral vessels.[8] More recently the pial vessels of patients who had cerebral vascular accidents were observed through burr holes, and it was seen that block-

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ing the stellate ganglion caused dilation of the pial vessels of the same side.[9]

The evidence that the degree of vasomotor control exercised by the sympathetic nerves is of clinical importance has been controversial. Results in animal experiments indicated that the circulatory change mediated by the vasomotor nerves was minor and not nearly as significant a factor in regulating the cerebral blood flow as changes in the general circulation, e. g., blood pressure.[10] It is possible, however, that the changes in vasomotor physiology that follow a cerebrovascular accident are more pronounced or are of a somewhat different nature from that produced in the normal brains of laboratory animals by nontraumatic means.[11] The reports, previously mentioned, of improvement in the clinical status of patients with cerebral embolism or thrombosis who were treated with unilateral stellate block would seem to indicate that the intracerebral circulatory disorder is to an extent spread or maintained by impulses passing over the perivascular sympathetic nerves.

The procedure of stellate block is probably the safest and most convenient means of stopping conduction of sympathetic impulses to the carotid plexus and the intracranial arteries. The stellate ganglion lies near the junction of the body and the transverse process of the seventh cervical vertebra.[12] The anterior approach is only one means of reaching this ganglion but was the sole approach used in the course of the treatment given in cases reported in this series. In the approximately three months during which the following 44 cases were studied, more than 150 stellate blocks were performed on the neuromedical service in the treatment of these and other disorders without significant complications. More than three fifths of these 44 patients demonstrated objective evidence of clinical improvement within an hour after the first stellate block was given.

## METHOD

The skin of the neck is first prepared with antiseptic, and a drape is applied. A point is determined about 2 fingerbreadths superior to the sternal notch, just lateral to the trachea and medial to the great vessels and the inner border of the sternocleidomastoid muscle. A skin wheal is made there with 2 per cent aqueous solution of procaine hydrochloride. Next, a 22 gage needle without a stilet is inserted close to the edge of the trachea. The great vessels of the neck are retracted with the other hand. With the patient supine, the needle is directed posteriorly, perpendicular to the vertical axis of the vertebral column. The area to be infiltrated is near the lateral aspect of the seventh cervical vertebra. After bone is reached, aspiration is performed to determine whether a vessel, the lung or the spinal canal has been entered. Ten cubic centimeters of 2 per cent procaine hydrochloride solution is used to infiltrate the ganglion, and if the injection is successful a Horner's syndrome will be produced within one to twenty minutes.

A preliminary intramuscular injection of 2 grains (0.13 Gm.) of phenobarbital sodium is given all conscious patients, a necessary precaution because of the possibility of a convulsion due to the stimulating action of 200 mg. of procaine hydrochloride.

In the present study veins were entered in a few instances, but the approach was remade without incident. In 1 case a small hematoma developed, probably following the accidental piercing of the vertebral artery, which runs near the stellate ganglion. However, the hematoma soon disappeared. Neither the pleural cavity nor the spinal canal was penetrated, and the likelihood of such an occurrence was believed slight.

The successful production of a Horner's syndrome in this series in which blocks were done by persons other than anesthetists was over 95 per cent. The high rate of success may have been due to the fact that 10 cc. of fluid spreads widely along the narrow fascial sheaths in the neck. It is probable that the use of a longer acting anesthetic would have been desirable, but such an anesthetic was used in only 2 instances.

Additional procaine was given intravenously to a few patients. The dosage was 500 mg. procaine hydrochloride in 500 cc. of 5 per cent dextrose solution administered in about two hours. This injection was always started at least an hour after the first stellate block and therefore did not affect the evaluation of the immediate response. It is impossible to say what the effects of the intravenous procaine were.

Before any patient received treatment a lumbar puncture was performed to aid in ruling out the presence of an intracerebral hemorrhage. In all cases a detailed neurologic examination was performed in order accurately to localize the lesion.

## RESULTS

Tables 1 to 3 record the clinical results. For convenience the cases were numbered according to their etiologic classification and the time that elapsed between the onset of symptoms and the first stellate block. The improvement noted, unless otherwise specified, was observed in fifteen minutes to an hour after the stellate block and retained for at least several days. The long term results were not evaluated, as the aim of this study was to determine whether or not this procedure was of immediate therapeutic value.

Each of the 28 persons who manifested what was interpreted as a favorable change in his clinical status demonstrated an increase in motor power or better speech that was apparent to several observers.

The most pronounced changes noted, however, were an increase in alertness and an improvement in behavior retained during the period of observation (at least several days). Many of these persons became able to feed themselves and were more careful of their excreta. Some regained their good spirits, whereas they had previously been dull and inattentive. Such improvements are readily subject to individual interpretation and were therefore evaluated with caution.

The results were usually considerably better in those patients who received treatment within a few hours after the onset of their symptoms. Hence, every effort was made to shorten the time interval between the onset and the initial stellate block. No patient was given treatment, however, unless a history of the course was previously obtained or at least an hour's observation was made to determine whether or not rapid and spontaneous improvement was taking place. No person who was recovering was treated.

The type of lesion seemed to be as important in influencing the outcome as the time interval that had elapsed between onset and treatment. Although there

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TABLE 1.—*Clinical Results with Stellate Ganglion Block in the Treatment of Acute Cerebral Thrombosis and Embolism*

| Case | Age | Sex | Diagnosis and Etiology * | Block-Time † | Results |
|---|---|---|---|---|---|
| | | | **Uncomplicated Thromboses** | | |
| 1‡ | 70 | M | Left M. C. | 2½ and 14 hr. | Improved after each block |
| 2 | 58 | M | Left Ant. C. | 3 hr. | Improved |
| 3‡ | 68 | M | Right M. C. | 5 and 24 hr. | Improved and regressed; improved |
| 4‡ | 67 | M | Left M. C. | 6 and 18 hr. | Improved after each block |
| 5 | 74 | M | Left M. C. | 7 hr. | No improvement |
| 6 | 70 | F | Right M. C. | 8 hr. | No improvement |
| 7 | 42 | M | Left M. C. | 11, 18 and 24 hr. | Improved |
| 8 | 64 | M | Left M. C. | 12 hr. | Improved |
| 9 | 61 | M | Right M. C. | 17 hr. | Improved |
| 10‡ | 62 | M | Left M. C. | (?)24 hr.; repeated on alternate sides every 12 hr. for 4 days | Improved after first block, gradually next 4 days and then less rapidly |
| 11 | 53 | M | Left M. C. | 21 hr. | Improved |
| 12 | 70 | M | Angular Br. Left M. C. | 24 hr. | No improvement |
| 13 | 58 | M | Right M. C. | 24 hr. | No improvement |
| | | | **Thromboses with Complications** | | |
| | | | **A. Multiple Thromboses (Both Old and New Lesions)** | | |
| 14‡ | 42 | M | Right M. C. | 5, 11 and 17 hr. | Improved only after first block |
| 15 | 56 | F | Left M. C. | 8 hr. | No improvement |
| 16 | 74 | F | Left M. C. | About 11 hr. | No improvement |
| 17 | 67 | F | Bilateral lesions | 3 wks. | No improvement (course halted) |
| | | | **B. Thromboses (Associated Cardiac Decompensation)** | | |
| 18‡ | 53 | F | Left M. C. | 5 hr. | No improvement |
| 19 | 71 | M | Right M. C. | 5½ hr. | Improved |
| 20 | 57 | M | Left M. C. | 11 and 24 hr. | Improved after each block |
| 21 | 69 | M | Left M. C. | 12 hr. | Improved |
| 22 | 70 | M | Left M. C. | 12 and 24 hr. | No improvement |
| 23 | 75 | M | Right M. C. | About 16 hr. | No improvement |
| 24 | 76 | F | Left M. C. | 24 hr. | No improvement |
| 25 | 77 | F | Right M. C. | 48 hr. | No improvement |
| | | | **C. Thrombosis (Suspected Rheumatic Brain Disease)** | | |
| 26‡ | 48 | F | Left M. C. | About 24 hr. | No improvement |
| | | | **D. Thrombosis (Associated Polycythemia)** | | |
| 27 | 7 | F | Right M. C. | About 48 hr. | Improved |
| | | | **E. Thromboses with Gradual Progression** | | |
| 28 | 51 | M | Left M. C. | 4 days | Improved; no regression |
| 29 | 79 | M | Right M. C. | 3 wks. | Improved; no regression |
| 30 | 65 | M | Right M. C. | 3 wks. | Improved; no regression |
| | | | **F. Thromboses with Syphilis** | | |
| 31 | 69 | M | Left M. C. | 16 and 24 hr. | Improved, then regressed |
| 32 | 53 | M | Left M. C. | 26 hr. | No improvement |
| 33 | 50 | M | Right M. C. | 2 days | No improvement |
| | | | **Hemiparesis After Ligation of Internal Carotid Artery** | | |
| 34 | 59 | F | Left hemiparesis | 36 hr. | Improved |
| | | | **Cerebral Vasospasm (Probable)** | | |
| 35 | 65 | M | Recurrent aphasia | 4 hr. | Improved |
| 36 | 66 | M | Recurrent hemiparesis | 2 wks. | Improved; attacks ceased |
| | | | **Cerebral Embolism** | | |
| 37‡ | 30 | F | Right M. C. | 2, 6 and 24 hr. | Improved after each block |
| 38‡ | 53 | F | Right M. C., multiple previous emboli | 4, 10, 16 and 24 hr. | In shock; appeared terminal; improved for a few days |
| 39 | 40 | F | Left M. C. | 8 and 24 hr. | Improved after each block |
| 40 | 48 | F | Left M. C. | 8 hr. | No improvement |
| 41 | 69 | M | Left M. C. | 15 and 24 hr. | Improved after each block |
| 42 | 65 | F | Multiple emboli | 30, 42 and 48 hr. (alternate sides) | Improved after each block |
| 43 | 32 | F | Left M. C. | 35 hr. | Improved |
| 44 | 36 | F | Right M. C. | 36, 40 and 50 hr. (alternate sides) | Improved after each block. Later a small cerebral abscess developed |

* M. C. refers to the middle cerebral artery.
† Time between onset of symptoms and the stellate block.
‡ Patient received procaine hydrochloride intravenously.

were too few cases in each of the etiologic categories into which the group was divided to permit definite conclusions to be drawn, a few tentative impressions were formed.

There were 5 persons who had had intracerebral vascular lesions prior to the present episode. Their response was rather poor. There were 8 patients with thromboses who had cardiac decompensation. Only 3 improved, although 7 were given treatment within twenty-four hours of the onset of their cerebral symptoms. Nine of 11 patients with uncomplicated cases of thrombosis treated within the same interval improved. The contrasting results are not surprising, since cardiac decompensation may be one of the precipitants of cerebral thrombosis.

TABLE 2.—*Clinical Results*

A. Comparison of Result with Time Between Onset and the First Stellate Block

| Hours | Patients Improved | Patients Unimproved |
|---|---|---|
| 0 to 6 | 9 | 1 |
| 7 to 12 | 5 | 6 |
| 13 to 24 | 5 | 5 |
| 25+ | 9 | 4 |
| Total | 28 | 16 |

B. Results of Treatment Within 24 Hours of Onset in Uncomplicated Cases

| | Patients Improved | Patients Unimproved |
|---|---|---|
| Thromboses (uncomplicated) | 9 | 2 |
| Embolism | 4 | 1 |
| Total | 13 | 3 |

TABLE 3.—*Notable Changes Observed in the 28 Patients Who Improved After Treatment*

| Observation | Number of Cases |
|---|---|
| Increased alertness | 27 |
| Greater motor power | 22 |
| Improved speech | 10 |
| Better comprehension | 8 |
| Less sensory deficit | 4 |
| Transient hyperesthesia | 2 |
| Loss of denial of limb | 2 |
| Loss of conjugate deviation of eyes | 2 |

After treatment all 3 patients whose symptoms had been progressive became significantly better and showed no further decline. The benefit occurred although they received their first stellate blocks from four days to three weeks after the onset of symptoms. It seemed remarkable that patients with symptoms of such duration showed any rapid change for the better.

The most encouraging results were obtained in cases of embolism. The group who had intracerebral emboli were on the average younger, and no doubt this may have been a favorable factor. Whether or not the results in comparable groups with thrombosis or embolism would be different is impossible to say.

The paralysis of the cervical sympathetic nerves by procaine block in the region of the stellate ganglion (as manifested by Horner's syndrome) usually did not last at the maximum more than a few hours. It seemed reasonable, therefore, to perform repeated blocks when progression of the illness occurred or in the attempt to gain additional benefit.

It is believed that the present therapeutic regimen may be somewhat inadequate because of the relatively short duration of the block used. It is probable that an evaluation of the long term results will be possible only when an effective, long-acting, local anesthetic is used and criteria established to determine the optimum number of blocks needed by any particular patient. The following cases illustrate the problem encountered.

Each patient in cases 1 and 3 had had a thrombosis of a middle cerebral artery and received a stellate block within a few hours of the onset. Both had an increase in motor power, became more alert and had better comprehension of what was said. One patient (case 1) was treated within two and one-half hours of the onset and had additional improvement within an hour after a second block performed about twelve hours later. The second patient (case 3) was treated five hours after onset but lost some of the improvement overnight. However, the lost ground was regained after

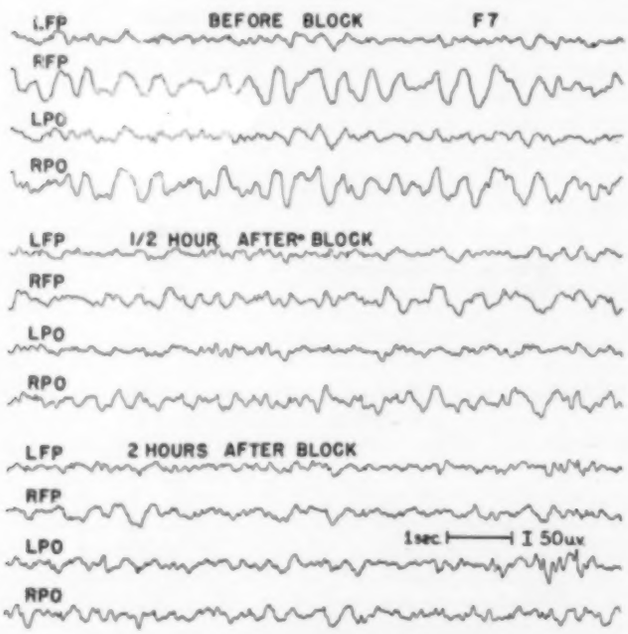


Fig. 1 (case 27).—Electroencephalogram before a right stellate block. There were slow (delta), high voltage waves recorded continually from the right hemisphere. One-half hour after the block the slow waves were of lower voltage. Two hours after the block, the slow waves were still present but occurred only intermittently and were generally of lower voltage. However, the same low waves that were present continually before the block occasionally returned.

another block, nineteen hours after the first. Each patient maintained his improvement for about four days, when the symptoms and observations originally present began to recur. Each died several days later. No further stellate blocks were given these patients, because early in the course of the study the need for repeated blocks was not fully appreciated.

In contrast to the foregoing is the favorable result in the following case, when the treatment was repeated.

Case 27.—A Mexican girl aged 7 had a tetralogy of Fallot. She had had secondary polycythemia for a number of years. At the time of her hospital admission (twelve hours after the first signs of hemiparesis), a left-sided weakness was perceptible but she was alert. Within the next twenty-four hours the hemiparesis became more decided, and she could be aroused only by painful stimulation. After the first block she became more alert, ate and moved the leg better. She improved for about twenty-four hours and then again became increasingly drowsy. At that time the block was repeated, and six to eight hours later the stellate ganglion on the side opposite the lesion was blocked. The following morning the procedure was repeated, this time on the same side as the lesion. She became more alert and stronger and during three weeks of further observation continued to gain. Adequate hydration during her hospital stay no doubt also played a part, but improvement in her clinical status was observed within an hour after each of the first two stellate blocks. Rapid changes were also noted in the electroencephalogram (fig. 1).

The repeated stellate blocks seemed to be a major factor in the reversal of the unfavorable course in the case of the foregoing patient, and in retrospect it was seen that in cases 1 and 3 the patients should have been treated with the same persistence.

Two patients with cerebral embolism (cases 37 and 39) had the sudden onset of a complete hemiplegia. They received blocks shortly after the onset, and two months later there were no residuals of the vascular accident. Such final end results have been duplicated in instances in which treatment therapy has not been given. However, each manifested a decided change for the better within a few minutes after the first stellate block.

Case 37.—A white woman aged 30 had rheumatic heart disease with auricular fibrillation. She was hospitalized because of embolism in the abdominal region. Two hours after the later onset of a left hemiparesis with anosognosia and denial of limb, a stellate block was performed. Within fifteen minutes she was aware of the paralysis, recognized her left arm and began to gain in strength. In the next twenty-two hours two additional blocks were performed on alternate sides. She regained most of her motor power in a few days, and two months later there were no signs of the cerebral embolism.

Table 4.—*Correlation Between Electroencephalogram and Clinical Status of Patient After Stellate Block*

| Case | Degree of Improvement | |
|---|---|---|
| | Electro-encephalogram | Clinical Status |
| 2 (fig. 2) | Marked | Moderate |
| 25 | None | None |
| 27 (fig. 1) | Moderate | Moderate |
| 31 (fig. 4) | Moderate | Moderate |
| 34 (fig. 3) | Minimal | Moderate |
| 36 | Minimal | Moderate |
| 42 | None | None |

Two patients in this series had had recurrences of a cerebral disturbance believed due to spasm of branches of the middle cerebral artery.

Case 36.—A man aged 66, who had been well except for hypertension, began to suffer from recurrent episodes of hemiplegia two weeks before he was admitted to the hospital. The duration of the paralysis varied from ten minutes to three days, and at times there were recurrences almost every hour. For several days before he was brought to this hospital he had had a residual right-sided weakness that failed to disappear between the attacks. Examination disclosed a blood pressure of 200 systolic and 100 diastolic. There were many more hemorrhages and exudates in the left fundus than in the right. He was dysarthric, could not elevate the right arm and was inattentive. Within a few minutes after a left stellate block the dysarthria had disappeared, he could hold his right arm over his head and he was more alert. The following day another block was performed and the patient improved. During the next two weeks he continued to gain ground.

In 1 instance a stellate block relieved a left hemiparesis that followed a ligation of the right internal carotid artery.

CASE 34.—A white woman aged 59 had had her right internal carotid artery ligated to prevent further hemorrhage from an intracranial aneurysm which could not be removed. About a day and a half after the ligation, a progressive left hemiparesis developed and she became increasingly drowsy. Thirty-six hours after the onset of these symptoms a right stellate block was performed. Within a few minutes she became much more alert, conversed and could keep her left arm elevated. Previously she had not been able to raise it from the bed. The patient continued to improve and was discharged five weeks later with only slight residuals.

### CHANGES IN THE ELECTROENCEPHALOGRAM FOLLOWING STELLATE BLOCK

An electroencephalogram [13] was recorded in 7 cases immediately prior to the first stellate block. Further recordings were made as soon as signs of Horner's syndrome appeared to indicate that the block had been successful. Others were made at intervals over the course of one or two hours.

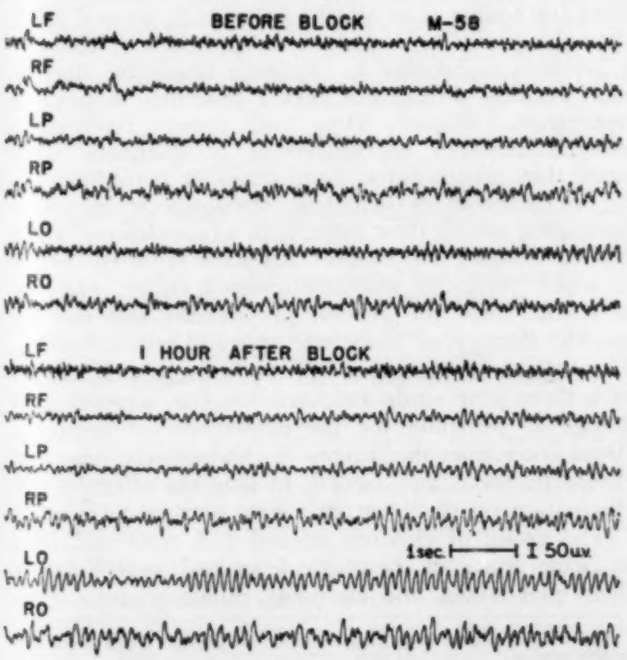


Fig. 2 (case 2).—Electroencephalogram before a left stellate block. The entire record was ragged. Some alpha waves were discernible in the right hemisphere, but there were few if any in the left hemisphere. One hour after the block the alpha activity was more prominent in all leads. The greatest return had occurred in the left parieto-occipital lead.

The correlation between the change in the electroencephalogram and the clinical status was only moderately good (table 4). Four of the tracings are illustrated. In case 2 the electrical record improved almost to normal (fig. 2). The patient, who had had a right hemiparesis most severe in the leg, regained almost all of the strength he had lost in his arm but retained the almost total paralysis of the leg. However, he lost the hypesthesia present only in the latter extremity.

In case 34 the patient showed an easily recognizable change for the better in the clinical state, but the electroencephalographic improvement (fig. 3) was slight and not noticeable except in the comparison of longer records than are illustrated here. In the other 5 patients the alterations or lack of alterations in the electroencephalograms were approximately paralleled in the clinical status (fig. 4).

Where improvement in the electroencephalogram occurred, the more normal waves appeared inter-

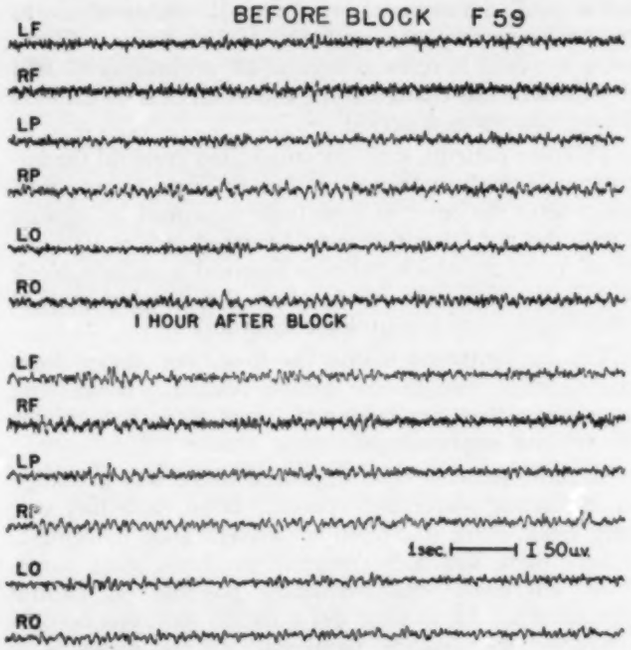


Fig. 3 (case 34).—Electroencephalogram before a right stellate block. One hour later there was only a little more alpha rhythm present in the entire record. However, this change was more apparent in the standard tracing than in the short section shown above.

mittently at first. In leads in which alpha activity had disappeared that type of activity first began to return about fifteen minutes after the first stellate block. As the record continued the alpha activity generally became

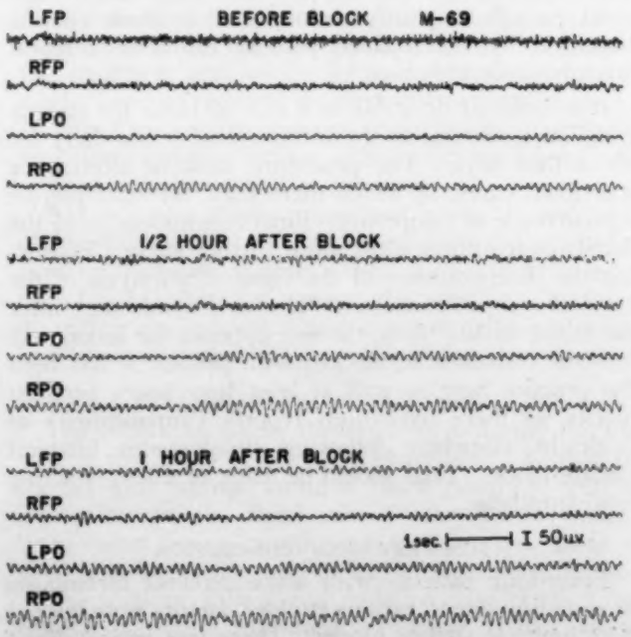


Fig. 4 (case 31).—Electroencephalogram before a left stellate block. There were no alpha waves apparent in the left parieto-occipital lead. One-half hour after the block, alpha waves appeared intermittently in the same lead. One hour after the block, the alpha rhythm was stable and the waves were of approximately the same amplitude and frequency as those of the opposite hemisphere.

more constant. The abnormalities disappeared or became less pronounced in the same manner.

13. The electroencephalograms were recorded and interpreted by Dr. A. Marianacci of the Los Angeles County Hospital (Medical Unit), Department of Electroencephalography.

### COMMENT

Of the 44 patients treated with stellate blocks 28 showed clinical improvement within fifteen minutes to an hour. Where there are many variables, as was the case in this present study (differences in age, type of lesion and duration of symptoms), statistics as to eventual recovery are probably of less value. However, it would have been beyond all probability to find any spontaneous change in the condition of such patients during this short a period.

Thirteen patients with uncomplicated cerebral thrombosis or embolism treated within the first twenty-four hours after the onset of symptoms improved, as against 3 who did not. Improvement occurred in 9 of 10 cases of all types in which patients received a stellate block within the first six hours after the development of manifestations of a neurologic disorder.

The improvement within the first hour varied from one third to two thirds toward normal. It was the impression that the milder the symptoms the greater the relative improvement.

In most patients who improved there was a change in the motor power and speech. If an extremity was only weak, there was often subsequent good movement. Where there had been complete paralysis, mass movement afterward was frequently possible on painful stimulation. At no time did a flaccid paralysis become converted to a spastic paralysis. In the presence of complete motor and sensory aphasia the patient often gained enough improvement to talk in paraphasia and jargon. Where the asphasia was primarily motor, understandable speech sometimes resulted.

The benefit to the patient was outstanding in a few instances, and the good results in the group far outweighed the trouble or risk involved. The changes noted and held during the period of observation were great enough to justify making stellate block routine treatment by well trained persons for acute cerebral thrombosis or embolism.

It is believed desirable as a rule to block the stellate ganglion ipsilateral to the intracerebral lesion daily for about four days. The procedure must be altered for individual cases, in which there may, for example, be a recurrence of symptoms. Final conclusions as to the details of treatment must await further study. Following the disappearance of the signs of paralysis of the cervical sympathetic chain (Horner's syndrome) after the initial stellate block, the side opposite the lesion may in some instances be blocked with profit. It has been the practice here to wait at least four hours between blocks, as there have been reports (unpublished) of 2 deaths elsewhere following simultaneous bilateral stellate block. Trial should be made of a longer-acting local anesthetic.

### SUMMARY AND CONCLUSION

Forty-four patients with acute cerebral thrombosis or embolism due to various etiologic factors were treated with multiple stellate blocks. There was improvement in 28 of 44 cases and in 9 of 10 with treatment within the first six hours after onset. In 5 of 7 instances there was improvement in the electroencephalogram following the first stellate block. Stellate block, a relatively innocuous procedure, is yet the most effective treatment of acute cerebral embolism or thrombosis.

## ORAL PENICILLIN PROPHYLAXIS OF RECURRENCES OF RHEUMATIC FEVER

### Interim Report on Method After a Three Year Study

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and
HELEN MacLEAN, A.B.
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It is generally believed that Lancefield group A hemolytic streptococci are involved in all or part of the pathogenesis of rheumatic fever.[1] Although penicillin is an unsatisfactory therapeutic agent for this disease,[2] this antibiotic should be excellent for prophylaxis of recurrences because of its ability to control the hemolytic streptococcus in vivo. This use of penicillin has been "mentioned hopefully" in the literature since 1946.[3] The relative infrequency of complications and sequelae are obvious advantages of penicillin in addition to its low toxicity in large dosages.[3a] Since penicillin, like the sulfonamide drugs, apparently fails to influence the onset and course of an attack of rheumatic fever if given after the preceding hemolytic streptococcic infection,[3a] it becomes mandatory to eliminate hemolytic streptococci entirely during the period preceding a possible recurrence. Massell, Dow and Jones [4] reported a lowered incidence of recurrences of rheumatic fever when they administered large doses of penicillin during an outbreak of hemolytic streptococcic infections developing among their patients in a convalescent home. Hofer,[5] Maliner and others [6] also have reported studies in which penicillin was administered either orally or in troche form for general prophylaxis and not for specific therapy of hemolytic streptococcic infections. The purpose of this paper is, first, to present the results of a three year study to determine the optimum oral dosage of penicillin for the elimination of hemolytic streptococci from the throats of children who have had rheumatic fever, and second, to note the effect of this elimination on the recurrence rate of rheumatic fever.

The group of children studied had recovered from an acute attack of rheumatic fever and were living in their own homes and attending public school. They

Dr. Stanley Gibson is the consultant for the Chicago Heart Association on this project.

Dr. Deborah V. Dauber, Department of Cardiovascular Research, Michael Reese Hospital, deceased, initiated the study.

Clara I. Jones, P.H.N., and Maria Heiser, P.H.N., school nurses of the Board of Health, Chicago, served throughout the study.

From the Chicago Heart Association and the Department of Bacteriology and Virology, Medical Research Institute, Michael Reese Hospital.

Supported by the Chicago Heart Association Memorial Fund, founded in memory of Morris Fishbein Jr., the Chicago Heart Association and the Michael Reese Research Foundation.

Valuable assistance was also given by: Dr. Hugh McCulloch, medical director of the Council on Rheumatic Fever of the Chicago Heart Association; Dr. Louis N. Katz, director of the Cardiovascular Research Department, Michael Reese Hospital; Dr. Herold C. Hunt, superintendent of the Board of Education; Mary E. Courtenay, assistant superintendent in charge of special education of the Board of Education; the principals of the schools involved; the staff and volunteers of the Chicago Heart Association, and the physicians of the children studied.

1. (*a*) Hench, P. S.; Bauer, W.; Boland, E. W.; Crain, D. C.; Freyberg, R. H.; Graham, W.; Holbrook, W. P.; Lockie, L. M.; McEwen, C.; Rosenberg, E. F., and Stecher, R. M.: Rheumatism and Arthritis: Review of American and English Literature of Recent Years, Ann. Int. Med. **28**: 93-110 (Jan.-Feb.) 1948. (*b*) Coburn, A. C., and Young, D. C.: The Epidemiology of Hematolytic Streptococcus, Baltimore, Williams & Wilkins Company, 1949, p. 170.

2. Rosenberg, E. F., and Hench, P. S.: Recent Advances in the Treatment of Rheumatic Fever, with Special Reference to Sulfonamide Prophylaxis and Intravenous Salicylate Therapy, M. Clin. North America **30**: 489-509 (May) 1946. Hench and others.[1a]

3. (*a*) Primer on the Rheumatic Diseases, report prepared by a Committee of the American Rheumatism Association, J. A. M. A. **139**: 1075-1076 (April 16) 1949. (*b*) Footnote 2.

4. Massell, B. F.; Dow, J. W., and Jones, T. D.: Orally Administered Penicillin in Patients with Rheumatic Fever, J. A. M. A. **138**: 1030-1036 (Dec. 4) 1948.

5. Hofer, J. W.: Oral Penicillin for Children with Rheumatic Fever, J. Pediat. **35**: 135-144 (Aug.) 1949.

6. Maliner, M. M.; Amsterdam, S. D., and Arreche, C. C.: Further Studies on Oral Penicillin in the Prophylaxis of Recurrent Rheumatic Fever, J. Pediat. **35**: 145-150 (Aug.) 1949.

present a different problem from that of children residing in the controlled atmosphere of the hospital or convalescent home, not only because they are exposed to infections prevalent in the general community but because medical care, especially of seemingly mild upper respiratory infections, is frequently neglected or delayed. In addition, the parent must cooperate in the administration of the prophylactic medicament. Therefore the method of administration must be one which a layman can follow easily. Furthermore, the medicament itself must be pleasant and well tolerated, as the successful prophylaxis of rheumatic fever must be continued for a long time. This paper is a progress report of the use of such a method, which was evolved after two years of controlled administration of penicillin in conjunction with bacteriologic study of throat cultures.

## PLAN OF STUDY

One hundred and twenty-six children attending a special public school in Chicago for children with rheumatic heart disease were studied for three successive school years representing three rheumatic fever seasons.[7] Eighty per cent had had an attack of rheumatic fever within the preceding year. None had his most recent attack longer than three years before the beginning of the present study, which was initiated in the autumn of 1946. None was taking any prophylactic agent. The children were divided into two groups, the division being selective only in that sex, race, age (range 6 to 14 years) and economic level were carefully considered so that equality was maintained in the two groups. All the children were being followed either in free clinics or by private physicians. One group served as a control and is referred to as control group 1. The other group received oral penicillin tablets[8] in varying dosages to be described. In addition, a second control group of 80 children of the same age and economic levels attending a similar public school for children with rheumatic heart disease was observed during the three year period. They are referred to as control group 2. These children were not in contact with any group receiving prophylactic medication.

Blood penicillin levels could not be determined because facilities were not available for such studies in public school children.

TABLE 1.—*Detailed Instructions to Parents of Children Receiving Penicillin Prophylaxis*

On school days, please give your child these tablets according to this schedule:

Two tablets on arising, at least one-half hour before breakfast
Two tablets before supper, at least one-half hour before eating
Two tablets at bedtime, at least two hours after eating

On Saturday and Sunday:

Two tablets on arising, at least one-half hour before eating
Two tablets before lunch, at least one-half hour before eating
Two tablets before supper, at least one-half hour before eating
Two tablets at bedtime, two hours after eating

We are only going to give these tablets the first week of each month, so please try to give us your complete cooperation. It is important to give the tablets on an empty stomach, that is, at least two hours after eating or drinking anything, except water. Also it is very important that your child receive his eight tablets every day for seven consecutive days. If he is going to be absent, please notify the school nurse at once.

*First Year.*—Sixty-four children received a 50,000 unit tablet of penicillin orally twice a day for five months during the first school year. This was administered by the school nurse two hours before lunch and two hours after lunch. On week ends the tablets were sent home with the proper instructions for the parent to administer the penicillin. Throat cultures, taken at the end of four months of daily penicillin on this schedule, revealed beta hemolytic streptococci in 17 of 64 cultures (26.6 per cent) in the daily penicillin group, compared with 10 of 50 (20 per cent) in the control group. Because we believed then that this regimen might be establishing penicillin fastness,[9] it was decided to change the mode of administration.

*Second Year.*—One million units of penicillin were given every day for five consecutive weekdays during the second school year as follows: two 100,000 unit tablets five times a day: one-half hour before breakfast, midmorning, two hours after lunch, one-half hour before supper and at bedtime. The parent was given proper instructions for the first, fourth and fifth doses, while the nurse gave the second and third doses at school and distributed the tablets for the remaining dosages. This five day course, amounting to a total of 5,000,000 units of orally given penicillin, was repeated five times at varying intervals throughout the autumn, winter and spring. The interval between courses was determined by the findings of throat culture studies.

Since the results of the second year indicated that maximum reduction in the incidence of throat cultures positive for hemolytic streptococci could be maintained for at least three weeks following the oral administration of this quantity of penicillin, it was decided to modify the dosage schedule again for the next school year.

*Third Year.*—Penicillin was given the first school week of every calendar month throughout the entire school year. Each course of penicillin amounted to 5,600,000 units, i. e., two tablets of 100,000 units each, given four times a day for seven consecutive days. Nine courses were given the first full school week of each month from October through June. To simplify the treatment and insure its being carried out accurately, parents received detailed instructions (table 1). A school nurse administered one dose and distributed the tablets and instructions. The tablets were swallowed at once and not sucked as troches.

A small part of the group was given an oral tablet of 250,000 units of penicillin[8] three times a day one-half hour before meals, making a total of 750,000 units a day or 5,250,000 units for a seven day course. There was no difference in results, and a tablet of larger dosage has an advantage in further simplifying the schedule.

## BACTERIOLOGIC STUDIES

The technic of taking throat cultures during the first year of this study is described elsewhere.[9] During the second year throat cultures were taken at varying intervals. In the third school year throat cultures were taken every month one to five days prior to the beginning of the week of penicillin administration.

The work of Pike[10] and more recently of the Commission on Acute Respiratory Diseases[11] substantiates our observation that plating of broth dilutions, rather

7. School year as used in this article refers to the nine months from September through June.

8. Buffered tablets of crystalline penicillin G potassium were supplied by Commercial Solvents Corporation (buffer consisting of glycerides and sodium salts of fatty acids).

9. Milzer, A.; Kohn, K. H., and MacLean, H.: Oral Prophylaxis of Rheumatic Fever with Penicillin, J. A. M. A. **136**: 536-538 (Feb. 21) 1948.

10. Pike, R. M.: An Enrichment Broth for Isolating Hemolytic Streptococci from Throat Swabs, Proc. Soc. Exper. Biol. & Med. **57**: 186-187, 1944.

11. Commission on Acute Respiratory Diseases: Problems in Determining the Bacterial Flora of the Pharynx, Proc. Soc. Exper. Biol. & Med. **69**: 45-52 (Oct.) 1948.

than direct throat swabs, resulted in a higher incidence of beta hemolytic streptococci, as well as a better selection of colonies for pure culture study. As in previous work,[9] the medium of choice was found to be Brewer's thioglycollate broth dispensed in test tubes. The technic included a preliminary six hour incubation period at 37 C., thorough mixing of the resultant minimal growth by rapid churning with the inserted swab, followed by streaking out a small loopful on citrated human blood agar plates. All plates were then incubated about fifteen hours at 37 C., and colonies were selected for further study.

Throat cultures were taken by one of us (K. H. K.) in exactly the same way and at the same time of day. The bacteriologic work was done by one person (H. M.) also in exactly the same way and by code number only, to eliminate bias.

Strains of beta hemolytic streptococci isolated during the second and third years of this study were typed with Lancefield group A, B and C streptococcic antiserums (Lederle), using the Lancefield precipitin technic.[12] Unfortunately we were unable to type the beta hemolytic streptococci isolated during the first year of this study, because Lancefield typing serums were not available at that time. The technic of the penicillin sensitivity tests used is the same as that described in a previous publication [9] except that veal infusion broth containing 1 per cent dextrose and added human erythrocytes (1 per cent) was used instead of ascitic dextrose broth.

## RESULTS OF BACTERIOLOGIC STUDIES

*Second Year.*—In bacteriologic studies a total of 326 throat cultures was taken from children in the penicillin-treated group at varying intervals after a course of penicillin therapy. In addition, 843 throat cultures were obtained from control groups 1 and 2 after the same intervals. It was found that September through December were months of low incidence of group A hemolytic streptococcic infection. This incidence slowly rose to a peak in February, when the penicillin-treated group had an incidence of 8.3 per cent three weeks after a course of penicillin. The incidence of the same organism in control group 2 in February was 28.9 per cent. In March the incidence began to decrease. At that time, two weeks after a course of penicillin, the treated group showed 5.4 per cent incidence compared to 28.5 per cent in control group 2. However, a similar period after a course of penicillin in a period of low incidence, as November, showed no infection in the penicillin-treated group and 13 per cent in control group 2. The incidence also decreased in March and April to a low in May and June which approximately equaled that of November. However, throat cultures from the penicillin-treated group in May, four weeks after a course of penicillin, given in April, still showed an incidence of 5.2 per cent compared with none in November in cultures taken two weeks after a course.

Control group 1 showed a similar fluctuation in positive cultures with a recognizable peak in February, but the incidence was less than that of control group 2. Perhaps the lower incidence of infection in control group 1 was due to the fact that these children were in contact with a penicillin-protected group rather than with unprotected children, as was control group 2 in the other school. Therefore, comparing the penicillin-treated group with control group 2, one observes that giving penicillin every two weeks apparently produces approximately 80 per cent reduction of infections with group A hemolytic streptococci during a period of high incidence in the community at large. The reduction was 100 per cent during a period of low incidence.

Throat cultures were made at longer intervals, such as four or six weeks after a course of penicillin, only in months of low incidence. One group showed good reduction and the other poor reduction. It was believed that these observations were not significant in view of the low incidence in the community at large. Since the cultures taken three weeks after a course of penicillin, at the peak of highest incidence, showed almost as good reduction (70 per cent) as those taken two weeks after a course (80 per cent), it was considered safe and more practical to wait three weeks between courses and to spread the dosages over seven days rather than to give a course of five days every two weeks. Thus the schedule of administration for the third year was determined.

*Third Year.*—Throat cultures were taken every month, one to five days before each seven day course of penicillin. A total of 914 throat cultures was studied, of which 346 were from the penicillin-treated group.

TABLE 2.—*Incidence of Group A Hemolytic Streptococci in Throat and Nose* Cultures of Penicillin-Treated Group and Control Groups of Children with Rheumatic Fever*

| Cultures Taken Prior to Course of Penicillin Given First Week of: | Penicillin Group | Control Group 1 | Control Group 2 | Normal Children |
|---|---|---|---|---|
| January | 0 | 0 | .. | .. |
| February | 14.2% | 22.2% | .. | .. |
| March | 0 | 7.8% | 20% | .. |
| April | 0 | 3.1% | 18.9%† | 16%‡ |
| May | 0 | 6.4% | .. | .. |
| June | 2.8% | 7.6% | .. | .. |

* Nose cultures were taken only in April, May and June.
† Cultures taken April 22.
‡ Based on 125 nose and throat cultures.

Later in this study we noted accidentally that there was little correlation between the incidence of positive nose cultures and positive throat cultures for group A hemolytic streptococci. For this reason an additional 400 nose cultures were taken from the various groups during the months of April, May and June. We also obtained nose and throat cultures from 125 non-rheumatic, presumably normal, school children of the same age group from a regular public school for comparison. The incidence of group A hemolytic streptococci is presented in table 2. The figures for January, February and March represent throat culture results only; all other figures are based on totals of throat and nose cultures. Had we taken nose cultures in January, the total percentages for January, February and March would undoubtedly have been much higher. The incidence in October, November and December, being either zero or so low as to be statistically insignificant, is omitted for simplification. Forty strains of beta hemolytic streptococci were isolated from nose cultures, of which thirty-two, or 80 per cent, were group A organisms. It is unfortunate that we were unable to obtain cultures regularly from control group 2, especially in February at the peak of highest incidence. We hope to remedy this situation in future studies.

As can be seen in table 2, penicillin given every fourth week for seven days completely eliminated group A hemolytic streptococci in every month but two. The high incidence in February is not surprising, in view of

12. Swift, H. F.; Wilson, A. T., and Lancefield, R. C.: Typing Group A Hemolytic Streptococci by M. Precipitin Reactions in Capillary Pipettes, J. Exper. Med. 78: 127-133 (Aug.) 1943.

the fact that this month was found to be the peak for both the second and third years. These results are in accord with those obtained by Coburn and Young [1b] in their studies of the epidemiologic basis of the hemolytic streptococcic infections in the Navy during World War II.

The over-all incidence of streptococcic infections was lower during the third than the second year, judging by the relatively few throat cultures positive for hemolytic streptococci that were obtained from control group 2. This lends support to our belief that the second year was apparently a severe one from the point of view not only of rheumatic fever recurrences (table 3) but also of group A hemolytic streptococcic throat infections.

*Penicillin Sensitivity Studies.*—Penicillin sensitivity assays were conducted on the two hundred and seventy-four strains of beta hemolytic streptococci isolated during the second and third years of study. The results obtained are outlined in table 4. The data of all three groups were pooled for tabulation, as there was no significant difference in sensitivity of strains of group A hemolytic streptococci isolated from the penicillin-treated group and from control groups 1 and 2. Most strains of group A hemolytic streptococci ranged in sensitivity from 0.005 to 0.08 Oxford units per cubic centimeter; while group B ranged from 0.04 to 0.15 units and group C from 0.01 to 0.08 units. These sensitivity figures are within the usual range of non-resistant strains as reported in the literature.[9] Therefore no evidence of significant increased resistance to penicillin was observed for hemolytic streptococci of group A, B or C during the second and third years of this study when large doses of penicillin were given orally, in contrast to the resistant strains isolated in the first year.[9]

TABLE 3.—*Percentage of Recurrences of Rheumatic Fever in Penicillin-Treated Children and Controls*

| | First School Year | Second School Year | Third School Year |
|---|---|---|---|
| Penicillin-treated group | 3% | 8% | 0% |
| Control group 1 | 5% | 13% | 11% |
| Control group 2 | 21% | 21% | 19% |

TABLE 4.—*Penicillin Sensitivity of 274 Strains of Beta Hemolytic Streptococci*

| Penicillin Sensitivity | Group A Strains | Group B Strains | Group C Strains | Other Strains |
|---|---|---|---|---|
| 0.005 | 4 | 0 | 0 | 0 |
| 0.01 | 45 | 0 | 3 | 1 |
| 0.02 | 71 | 0 | 22 | 7 |
| 0.04 | 9 | 2 | 6 | 4 |
| 0.08 | 16 | 28 | 2 | 14 |
| 0.15 | 4 | 30 | 1 | 3 |
| 0.31 | 0 | 0 | 0 | 0 |
| 0.625+ | 0 | 0 | 0 | 2 |
| Total | 149 | 60 | 34 | 31 |

*Other Bacteriologic Studies.*—One of us (K. H. K.) became interested in the possibility that *Candida albicans* might be a factor in rheumatic fever. Only the monthly nose and throat cultures of the third year were available for study, as other sites, such as the intestinal tract or the genitourinary tract, could not be investigated in these public school children. The incidence of C. albicans found in the group of 125 normal children in the early part of April was 11.2 per cent. In the two special schools with rheumatic children the incidence at this time (within a few days) was 23.6 per cent in the penicillin-treated group, 15.6 per cent in control group 1 and 26.9 per cent in control group 2. Cultures of material from children of these three groups taken at other times during the year were consistently higher in growth of C. albicans than the April low of 11.2 per cent found only in the normal group. Of 31 rheumatic children whose monthly throat cultures exhibited the growth of C. albicans at one time or another during the school year, 20 had this organism in three or more cultures. It is not intended to draw any inferences or conclusions from these data; it is reported here as an interesting incidental observation during our throat culture studies which perhaps merits further investigation.

### CLINICAL RESULTS

The percentage of recurrences of rheumatic fever during the three year study is shown in table 3. The total number of children in each group varied slightly each school year because of absences for nonrheumatic illness or personal reasons, transfer, graduation or new admissions. During the first year there were 64 children in the penicillin-treated group and 62 in control group 1. In the second and third years, when large doses were given, the number had to be reduced because of the limitation of penicillin available for this study. The penicillin-treated group averaged 48, control group 1 averaged 45 and control group 2 averaged 80.

The criteria for diagnosis of recurrences of rheumatic fever were elevated temperature, increased sedimentation rate, leukocytosis, typical symptoms of articular involvement and/or signs of cardiac involvement. No instances of chorea occurred. The diagnosis was verified on admission to recognized local hospitals whose records were available to us. The school nurses who administered the penicillin investigated all absences from school of more than three days in the penicillin-treated group and control group 1. Because of personnel difficulties at the other school, this could not be done for control group 2, but when a recurrence of rheumatic fever was diagnosed in this group one of us (K. H. K.) checked the source of the diagnosis. Possibly some recurrences were missed in this latter group, for, if the child was kept at home with another diagnosis, the absence was not reported to us.

The close supervision of the penicillin-treated group and of control group 1 which we were able to maintain during the second and third years of the study enables us to discuss the recurrences in these groups in some detail. These occurred one each in November and February, three each in December, January and April, and four in March. Similar supervision of control group 2 was impossible, therefore details of the recurrences are not reliable. Of the recurrences in the penicillin-treated group, 4 had had one previous attack, 2 had had two and 1, three previous attacks. In control group 1, 4 had had one, 6, two, and 2, three previous attacks.

The number of years elapsed since the last attack, whether it was the initial one or a previous recurrence, varied in both groups. In the penicillin-treated group it was one to three years, averaging two years. In control group 1, it varied more widely from one to seven years; in 2 cases within one year, in 4 within two years, in 2 within three years, in 1 each within four, five, six and seven years. Differences in age and sex were not significant.

The clinical course of the recurrences did not seem to be influenced either favorably or adversely by the taking of penicillin as prophylaxis. Some recurrences were mild and without immediate evidence of further cardiac damage; absence from school was for two or three months only. Others were more severe, necessitating long hospitalization or stay in convalescent homes. On returning to school after a recurrence, the child was included in his original group. There was 1 fatality—a child in the penicillin-treated group in the second year, who had had three previous attacks, became ill in February and died two months later in the hospital. The cause of death was reported as acute rheumatic pericarditis. Her last throat culture, taken before the last course of penicillin, revealed 40 per cent group A hemolytic streptococci with a penicillin sensitivity of 0.02 units. One child who had a recurrence in the fall of the third year, did not return to school but was taken to Arizona, where it was reported that she had another recurrence in April.

One would expect to find some correlation between the recurrences and the finding of group A hemolytic streptococci, especially during the third year, when throat cultures were taken with regularity before each course of penicillin. Two of the five children with recurrences had shown group A hemolytic streptococci in their most recent culture. Cultures taken during the second year were, of course, not so closely correlated. One child in control group 1 had 90 per cent group A hemolytic streptococci in a culture taken three weeks before the onset of recurrence, 1 in the penicillin-treated group had 20 per cent group A hemolytic streptococci five weeks before onset, and another in this group had 40 per cent group A hemolytic streptococci seven weeks before onset. Four of these five showing correlation between recurrences and positive throat cultures had recurrences in March following the high peak of incidence of group A hemolytic streptococci found in February of both years.

No child in this study experienced any difficulty in taking tablets of penicillin orally. Twenty-nine, or 58 per cent, have taken the penicillin for the entire three years of the study. One child was given treatment by his own physician for an allergic urticaria thought to be due to penicillin, but he continued his prophylactic courses without further reactions. In another study we have noted the occasional occurrence of urticaria, which was controlled by the use of antihistaminic drugs. No other reactions occurred.

## COMMENT

The recurrence rate of rheumatic fever in the penicillin-treated group was lower each year than that in the control groups. In the first and second years this difference is probably not significant, but in the third year it is more pronounced. We believe that the total absence of recurrences in the group taking penicillin in the third year is encouraging and merits continuation of the study, with the dosages and mode of administration as described.

One should note here that, although adequate statistics on the incidence of rheumatic fever in the general population are not available, the first year of our study was considered a light year while the second year was definitely one of high incidence for the disease. It is generally agreed that in the community at large in some years there is a higher incidence of rheumatic fever than in others. Adequate data are not yet available for the third year. Thus the higher recurrence rate found during the second year was to be expected. Since the penicillin was administered at intervals varying from two to six weeks and only five times during the entire nine month period, we now believe that protection was inadequate during this period. This was substantiated in the throat culture studies.

It was not possible to follow control group 2 as closely as control group 1, especially during the second and third years of the study. Presumably this group represents the normal recurrence rate during the first year of the study, but the rate of recurrence was probably higher than indicated herein for the second and third years, because all absences from school were not reported to us and diagnoses other than that of rheumatic fever were not checked. There was a decided difference in the rate of recurrence between the two control groups, for, although both groups are in similar special schools, one (control group 1) is in the same school as the penicillin-treated group. It is possible that by protecting part of the children in one school with penicillin, the incidence of infection was lowered and cross infection by contact during school hours was so decreased as to afford some protection to the control group in the same school.

The children in this study fall into the categories associated with a high rate of recurrence of rheumatic fever. They live in a large urban area and in medium to low income groups, which subjects them to crowded living conditions as well as questionable nutrition. They are in that age group which is most subject to frequency of recurrence. The probability of recurrence is increased greatly in the first year following an attack, and 80 per cent of this group had had an attack within one year of the beginning of the present study. Although they attend a special school which provides more protection than an ordinary one, the environment of these children after school hours is subject to all the danger of exposure to infection of the general population. Our observations during the school year covered both the autumn and spring seasons, which are the periods of highest incidence of rheumatic fever. Because of this increased incidence in the autumn and the fact that the children are returning to school, where they are in close contact with larger groups of potential carriers of infection than in the summer months, it is perhaps advisable to continue oral administration of penicillin prophylaxis throughout the entire calendar year. This would apply especially to children in poor general condition or to those living in particularly unfavorable localities with high rheumatic fever rates.[13]

It is possible that smaller doses of penicillin would be equally effective. However, in other instances in which we have observed high percentages of hemolytic streptococci in nose and throat cultures, it was found necessary to give large amounts of penicillin orally to eliminate the streptococci. Since the children in this study have taken those dosages for two years without reactions or complications, the administration of large doses of the drug for short periods of time is considered reasonably prudent.

The danger of the development of other penicillin-resistant organisms and the possibility of unknown sequelae to the taking of any drug for long periods of time are not to be overlooked. However, we believe that our method of administration has avoided these results so far and merits continuation of the study. Kerr

13. Holbrook, W. P.: Prevention of Rheumatic Fever, Chicago M. Soc. Bull. **51**: 158-161 (Sept. 4) 1948.

stated (referring to the sulfonamide drugs) "these risks should be taken in view of the danger of repeated insults to the heart." [14]

In addition, it is imperative that in any prophylactic method which conceivably would be used for successive months, if not years, the procedure be as simple as possible for the lay person to follow. In this instance the schedule followed during the third year of this study conforms to this requirement, for the parent can easily remember to give the tablets of penicillin orally before meals and at bedtime during the first week of every month.

SUMMARY

A feasible schedule of oral administration of penicillin consisting of 800,000 units daily for seven consecutive days the first week of each month throughout the school year has been shown to be effective in significantly reducing the incidence of hemolytic streptococcic infections in the throats of children who have had rheumatic fever.

Clinically, the recurrence rate of rheumatic fever was zero in the penicillin-treated group compared with 11 and 19 per cent in control groups 1 and 2, respectively, when this schedule of administration was followed during one complete rheumatic fever season. These observations are sufficiently encouraging to warrant continued study.

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## Clinical Notes, Suggestions and New Instruments

### AGRANULOCYTOSIS OF THE NEWBORN INFANT

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Agranulocytosis has been reported as occurring from infancy on through all age groups. However, we have been unable to find any reports of agranulocytosis of a newborn infant. In 1933 Givan and Shapiro [1] reviewed the cases of 2 infants, aged 10 and 12 weeks, with agranulocytosis. Ten years later Kato [2] reported the case of an 8 week old infant, in whom agranulocytosis developed during treatment with sulfathiazole. We present the history of a newborn infant who was found to have agranulocytosis on his third day of life.

REPORT OF CASE

M. C., a white male infant, was born on April 15, 1948, weighing 6 pounds 13 ounces (3,089 Gm.) and measuring 19.5 inches (49.5 cm.) in length.

The mother was 38 years of age. She had been pregnant twice but had carried no other child to term. The Wassermann reaction was negative, and her blood was type O and Rh positive. About one year before delivery she passed large clots of blood and thought she had been pregnant. Her past history did not reveal any serious illnessses, but she had had an operation on her neck for an enlarged gland at the age of 7. During her pregnancy, she was seen regularly by the obstetrician who delivered her, and no abnormalities were noted. Two hours and forty-five minutes before delivery she was given 50 mg. of meperidine hydrochloride (demerol hydrochloride®) and 1/150 grain (0.43 mg.) of scopolamine hydrobromide intramuscularly. The total period of active labor was six hours. During delivery the mother was under anesthesia induced with cyclopropane and the delivery was aided with a mediolateral episiotomy and outlet forceps but was otherwise uneventful.

The infant cried spontaneously; his color was good, and no abnormalities were noted. Several hours after his delivery feedings of a dilute evaporated milk formula were begun, which were taken well. At 2 p. m. on April 18, approximately seventy-five hours after delivery, it was noted that his temperature was 102 F., although he presented no unusual symptoms or physical findings.

At 7 p. m. that day the infant appeared listless and took only a small amount of formula. A blood cell count made at that time revealed that the hemoglobin was 109 per cent and that the red blood cells numbered 5,300,000 and the white blood cells 4,200 per cubic millimeter, with 1 per cent neutrophilic myelocytes, 1 per cent eosinophilic myelocytes, 41 per cent lymphocytes and 52 per cent mononuclear cells. Because of the unusual findings in the total and differential white cell counts, additional counts were made within two hours, and the same results were obtained. The infant was given 2 hypodermoclyses of 50 cc. each of Hartmann's solution, and penicillin therapy was started, 4,000 units every three hours. During the next twenty-four hours the infant's temperature was normal; he appeared well and took his feedings readily. The results of repeated physical examinations were normal. On the third day of illness the patient was fretful and refused feedings; his temperature ranged between 99 and 102 F. He was given hypodermoclyses of Hartmann's solution, and the dosage of penicillin was raised to 10,000 units every three hours. On the evening of this day he suddenly became markedly dyspneic and was placed in an oxygen tent, where the dyspnea was relieved. A roentgenogram of the chest showed consolidation of the upper lobe of the right lung. Roentgenograms of the long bones were normal. The dosage of penicillin was then raised to 20,000 units every three hours. On the following day, April 21, the infant's condition was still poor. He refused feedings, and his respirations were labored even while oxygen was being administered, but there was no cyanosis .

In the belief that there was a possibility of infection due to a penicillin-resistant organism, streptomycin therapy was started, 25 mg. every two hours. On April 22, during a feeding, the infant aspirated a small amonut of formula and became notably cyanotic. He was readily relieved by suction, and oral feedings were discontinued. A "cut down" was done on a vein of the ankle, and during that day he received 450 cc. of 5 per cent dextrose in isotonic sodium chloride solution and distilled water and 70 cc. of fresh whole blood intravenously. On April 23 the infant's general condition was improved. He was again fed by nipple and took the feedings without embarrassment. That day marrow aspirated from the left tibia was hypocellular and agranulocytic, with an absolute increase of progranulocytes, lymphocytes and monocytes. From April 23 until the morning of April 29 the infant's condition was good. On April 27 the streptomycin therapy was discontinued. A roentgenogram of the chest that day still showed increased density of the upper lobe of the right lung. On April 29, 70 cc. of citrated fresh whole blood was again given intravenously. Later that day the patient began to have labored respirations with substernal retractions. Auscultation of the chest revealed distant breath sounds over the left lung field. The respiratory rate varied between 80 and 96 per minute, and the temperature ranged from 100.2 to 102.6 F. The administration of streptomycin was started again, 20 mg. every two hours. By early morning of April 30 the infant's respiratory rate had come down to 54 a minute; his temperature was 99.4 F., and he appeared improved. Later that morning, aspiration of the tibial marrow was repeated, and the marrow showed the same composition as on April 23. Since the infant appeared improved, small amounts of formula were offered, and he took these readily, while the remainder of his fluid requirement was given intravenously.

14. Kerr, W. J.: Cardiovascular Diseases, J. A. M. A. **126**: 972-973 (Dec. 21) 1946.

From the Departments of Pediatrics and Obstetrics, New York Medical College, Flower and Fifth Avenue Hospitals.

1. Givan, T. B., and Shapiro, B.: Agranulocytosis in Childhood, Am. J. Dis. Child. **46**: 550 (Sept.) 1933.

2. Kato, K., and others: Fatal Agranulocytosis Following Sulfathiazole Therapy, J. Pediat. **22**: 432, 1943.

On May 1 his condition was sufficiently improved so that he was without oxygen for varying intervals of time. The dosage of streptomycin was reduced to 10 mg. every three hours and that of penicillin to 20,000 units every three hours. The infant continued to improve, and on May 4 he was able to be without oxygen therapy.

Complete blood cell counts were done daily from the onset of the infant's illness until his discharge (table). The granulocytopenia persisted until May 4, eighteen days after it was first noted, when the neutrophils rose to 19 per cent. From that day on the neutrophils approached normal values. It is interesting that from the day the neutrophils returned to normal values the infant began to eat well and show a sustained weight gain of 1 to 2 ounces (28 to 57 Gm.) daily. He remained afebrile and symptom free and was discharged on May 23, 1948, weighing 8 pounds 1 ounce (3.657 Gm.).

To rule out the possibility of blood dyscrasia in the mother, a complete blood cell count was done on April 18, and this was normal. A heterophilic antibody test of both the infant's and the mother's blood showed no agglutination. A culture of the infant's urine on April 21 grew Escherichia communior. Since the specimen was not obtained by catheterization, the pathogenicity of this organism in our case may be doubted. A blood culture made that day failed to grow any organisms.

*Daily Blood Cell Counts of Infant with Agranulocytosis*

| Date | 4/18 | 4/20 | 4/22 | 4/24 | 4/28 | 5/1 | 5/4 | 5/5 | 5/7 | 5/14 | 5/20 | 5/22 | 6/21 | 7/6 | 8/10 | 9/21 | 11/7 | 1/6/49 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hemoglobin, % | 109 | 98 | 102 | 113 | 109 | 152 | 144 | 140 | 144 | 110 | 105 | 101 | 65 | 64 | 81 | 85 | 91 | 75 |
| Erythrocytes, millions | 5,310 | 4,800 | 4,900 | 5,570 | 5,330 | 7,152 | 6,550 | 6,470 | 6,330 | 5,650 | 4,900 | 5,100 | 3,190 | 3,060 | 4,750 | 4,700 | 5,100 | 4,400 |
| Leukocytes | 4,200 | 3,550 | 6,500 | 11,100 | 11,050 | 6,400 | 12,450 | 16,700 | 22,000 | 14,950 | 10,600 | 8,800 | 7,550 | 5,800 | 3,750 | 6,800 | 9,200 | 8,200 |
| Neutrophils | 1 | 4 | 3 | 3 | 4 | 6 | 19 | 23 | 34 | 44 | 29 | 23 | 25 | 21 | 23 | 23 | 24 | 37 |
| Mature | (1) | (1) | (0) | (0) | (1) | (4) | ( 9) | (16) | (24) | (36) | (25) | (16) | (25) | (20) | (23) | (21) | (22) | (35) |
| Immature | (0) | (3) | (3) | (3) | (3) | (2) | (10) | ( 7) | (10) | ( 8) | ( 4) | ( 7) | ( 0) | ( 1) | ( 0) | ( 2) | ( 2) | ( 2) |
| Eosinophils | 1 | 2 | 6 | 8 | 4 | 5 | ..... | ..... | 2 | 5 | ..... | 1 | 3 | 2 | ..... | 5 | 2 | ..... |
| Basophils | ..... | ..... | ..... | ..... | 2 | ..... | ..... | ..... | ..... | 1 | ..... | ..... | ..... | 1 | ..... | ..... | ..... | ..... |
| Metamyelocytes | ..... | ..... | ..... | ..... | ..... | ..... | ..... | 4 | 5 | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| Myelocytes | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| Neutrophilic | ..... | ..... | 15 | 10 | 2 | 6 | 7 | 7 | 10 | ..... | ..... | 4 | ..... | ..... | ..... | ..... | ..... | ..... |
| Eosinophilic | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| Basophilic | ..... | ..... | 1 | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| Blast cells | ..... | ..... | 2 | ..... | ..... | ..... | 2 | ..... | 3 | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |
| Lymphocytes | 41 | 70 | 48 | 57 | 69 | 68 | 42 | 46 | 40 | 41 | 59 | 63 | 70 | 68 | 73 | 70 | 72 | 60 |
| Monocytes | 57 | 23 | 24 | 22 | 9 | 15 | 28 | 19 | 6 | 9 | 8 | 9 | 2 | 6 | 4 | 2 | 2 | 2 |
| Plasmacytes | ..... | 1 | ..... | ..... | ..... | ..... | 2 | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | 1 |
| Thrombocytes | ..... | 165,000 | ..... | ..... | ..... | ..... | ..... | 75,000 | 150,000 | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... | ..... |

From the time of discharge until he was 3 months of age the patient was seen at weekly intervals, during which time physical examinations failed to reveal any abnormalities and complete blood cell counts gave hemograms within normal limits. From that time until the present writing he was seen at monthly intervals. His growth and development have been normal. When the infant was 9 months of age, an examination of the marrow showed a differential myelogram which was normal for his age.

## COMMENT

According to most observers, agranulocytosis is primarily an involvement of the marrow with depression of formation or maturation of granulocytes. Many factors have been suspected of causing this change, and some of these are listed:

1. Severe sepsis, acute or chronic, which affects the myeloblastic tissue and depresses the formation of granulocytes.
2. Possible congenital absence in the marrow of a necessary factor which would make an individual susceptible to leukopenia.
3. Secondary neoplastic invasions of the marrow.
4. Agranulocytosis may be part of a blood dyscrasia.
5. A number of drugs have been known to act on the marrow and cause granulocytopenia. Among these are sulfonamides, arsenicals, gold compounds, barbiturates, quinine and many others known by proprietary names which contain the benzene ring as part of their chemical structure.
6. Endocrine disturbances have been known to cause agranulocytosis, and, of these, adrenal insufficiency more commonly.
7. An acute shocklike or anaphylactic manifestation, which could explain agranulocytosis in the first week of life. It has been suggested that the fetus becomes sensitized in intrauterine life by substances from the mother which pass through the placenta. During labor, many villi are torn, and a massive amount of these maternal substances come into the fetal circulation, which could cause a shocklike phenomenon.

It has been observed that newborn infants may present allergic symptoms from the fourth to the seventh day of life. Among these are erythema neonatorum, generalized lymphadenopathy and splenomegaly at the fourth day of life. At the same time there are changes in the blood picture, the most characteristic of which is eosinophilia from the fourth to the seventh day. This eosinophilia is often preceded by leukopenia of short duration. If the antigen-antibody reaction acts on the marrow, the effect may be an arrest of the release of mature cells to produce neutropenia, anemia or thrombopenia.

We feel that in our case none of the agents which more commonly cause agranulocytosis in older children and adults was responsible. The mother received no drugs, nor did she have any illnesses before delivery which may have caused the agranulocytosis. Her blood cell count showed no evidence of blood dyscrasia. If there were a congenital absence of a necessary factor or a hypoplasia of the bone marrow, one would expect the erythroid elements to be depressed. This was not seen in our patient. There were no obvious endocrine disturbances.

In our case the etiologic factor may have been sepsis, which was noted clinically first in the elevated temperature and irritability of the infant. Blood cultures, as have been noted, failed to grow any organisms. However, this does not exclude the possibility of sepsis. The pneumonias may be considered as later complications of the agranulocytosis. The concept of agranulocytosis as an anaphylactic or shocklike manifestation which occurs during the first week of life is most intriguing. At present we have no proof that this pathogenesis does occur.

Until the advent of antibiotics the therapy of agranulocytosis consisted in the use of many agents, none of which was singularly effective. The patients died of secondary infections which could not be controlled. Included in the therapeutic armamentarium were: yellow marrow, pentnucleotides® (a preparation of the sodium salts of the pentose nucleotides), whole blood, reticulogen® (a parenteral liver extract with thiamine hydrochloride added), liver extract, pyridoxine, vitamin B complex and, more recently, folic acid. In our case we gave fresh whole blood by transfusion, intravenous fluids, penicillin and streptomycin. We feel that only the fluids and the antibiotics were of definite value.

## SUMMARY

A case of agranulocytosis of a newborn boy is reported. The infant recovered, and his growth, development, bone marrow and blood are normal at present.

We believe that sepsis might have been the main etiologic factor. After intensive therapy with fluids, fresh whole blood and antibiotics, the sepsis was overcome and the marrow gradually resumed its normal function.

## Council on Physical Medicine and Rehabilitation

*This paper was prepared at the request of the Council and is one of a series appearing in* THE JOURNAL. *Later the entire series will appear in book form as the Council's Handbook of Physical Medicine and Rehabilitation.*

HOWARD A. CARTER, *Secretary.*

# MEDICAL DIATHERMY

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Medical diathermy is based on the use of high-frequency currents for the generation of heat in the tissues of the body for therapeutic purposes. The frequencies of the currents used are sufficiently high so that nerves or muscles are not stimulated. The intensity used is sufficiently low so that the temperature developed in the tissue is below that required to destroy the tissue or impair its vitality. The high-frequency currents used for diathermy can be applied locally for the purpose of heating the superficial and deep tissues.

Medical diathermy can be classified in the following 3 main divisions, based on differences in wavelengths and on the sources of the high-frequency current: (1) microwave diathermy; (2) short-wave diathermy and (3) long-wave diathermy. The table indicates the range and frequencies of wavelengths employed in the various divisions of the electromagnetic spectrum as it applies to diathermy. The Federal Communications Commission has assigned definite bands in the range of frequencies and wavelengths to the medical profession and to the manufacturers of diathermic equipment. All modern diathermic apparatus must meet the requirements for frequencies and wavelengths of the Federal Communications Commission. In addition to the band of 2,450 megacycles previously assigned for microwave diathermy, the following frequencies have been made available: 915 megacycles, 5,850 megacycles, 10,600 megacycles and 18,000 megacycles. The commission has also assigned the following 3 frequencies to manufacturers and users of apparatus for short-wave diathermy: 13.66 megacycles, 27.32 megacycles and 40.98 megacycles.

In considering, as a whole, the research work that has been done on the physiologic effects of diathermy, it can be stated that all physiologic effects which result from the use of medical diathermy are dependent on the heating effect of the high-frequency currents on the tissues. Therapeutic use of short-waves and microwaves indicates that there may be some selective heating of the various tissues. Selective heating with short-wave diathermy apparently is dependent primarily on the type of application used and the conductivity of the tissues; with microwaves it is apparently due to a selective absorption of the frequencies by the tissues.

The most recently developed portion of the electromagnetic spectrum for therapeutic use is that of the microwaves. Detailed data from experimental work have been accumulating during recent years, which evaluate the physiologic effects of microwaves on tissues of human beings and animals. Leden and associates [1] have studied the effects of microwaves on trained and anesthetized dogs and have shown definite increases in the temperatures of cutaneous and subcutaneous tissues and of muscle in the exposed region. The increase in temperature was accompanied by an increase in flow of blood. Worden and his associates [2] have shown increases in temperature of normal and ischemic tissues after exposure to microwaves. They have also reported that on exposure of 60 to 80 watts a maximal increase of temperature in muscle was obtained in twenty minutes and an increase in flow of blood followed; a decrease in temperature followed a thirty minute exposure to the microwaves. Gersten and his co-workers,[3] in similar studies on human beings, confirmed these findings of increases of temperature and flow of blood in extremities exposed to microwaves. Richardson, Duane and Hines [4] and also Daily, Wakim, Herrick and Parkhill [5] have shown that exposures of the eyes of animals to diathermy with microwaves may result in opacities in the lenses.

Clinical use of microwaves is only now beginning. However, careful clinical experience for a period of years, carried out by careful observers, will be required before the clinical status of diathermy with microwaves can be definitely established. Although the apparatus for diathermy with microwaves has been approved by the Council on Physical Medicine and Rehabilitation, definite care and precautions should be taken in its use which should be confined to members of the medical profession.

*Classification of Medical Diathermy According to Wavelengths and Frequencies*

| | Range | | F.C.C. Bands* | |
|---|---|---|---|---|
| Diathermy | Wavelength | Frequency, megacycles† | Wavelength | Frequency, megacycles† |
| Microwave | 1 mm.-1 m. | 300-300,000 | 12.2 cm. | 2,450 |
| Short-wave | 3-30 m. | 10-100 | 22.0 m. | 13.66 |
| | | | 11.0 m. | 27.32 |
| | | | 7.3 m. | 40.98 |
| Long-wave | 30-3,000 m. | 0.1-10 | ..... | |

* In addition the following frequencies may be used: 915 megacycles, 5,850 megacycles, 10,600 megacycles and 18,000 megacycles. The Federal Communications Commission (F.C.C.) has legally limited the use of medical diathermy to the frequencies shown.

† One megacycle equivalent to 1,000,000 cycles or 1,000 kilocycles.

Short-wave diathermy can be applied to the body by means of an induction cable which provides an electromagnetic field or by the use of condenser pads or air-spaced electrodes which provide an electrostatic field. Mittelmann and Holmquest [6] have shown that heating by means of an induction cable results in an increased rise of temperature in muscles and in highly vascular and conductive tissues, whereas the condenser type of application which provides an electrostatic field results in higher temperatures in the less highly conductive mediums, such as skin, fat and bony tissues. It is on this basis that the application of short-wave diathermy

1. Leden, U. M.; Herrick, J. F.; Wakim, K. G., and Krusen, F. H.: Preliminary Studies on the Heating and Circulatory Effects of Microwaves—"Radar." Brit. J. Phys. Med. **10**: 177-184 (Nov.-Dec.) 1947.

2. Worden, R. E.; Herrick, J. F.; Wakim, K. G., and Krusen, F. H.: The Heating Effects of Microwaves With and Without Ischemia, Arch. Phys. Med. **29**: 751-758 (Dec.) 1948.

3. Gersten, J. W.; Wakim, K. G., Herric, J. F., and Krusen, F. H.: The Effect of Microwave Diathermy on the Peripheral Circulation and on Tissue Temperature in Man, Arch. Phys. Med. **30**: 7-23 (Jan.) 1949.

4. Richardson, W. A.; Duane, T. D., and Hines, H. M.: Experimental Lenticular Opacities Produced by Microwave Irradiations, Arch. Phys. Med. **29**: 765-769 (Dec.) 1948.

5. Daily, L., Jr.; Wakim, K. G.; Herrick, J. F., and Parkhill, Edith M.: Effects of Microwave Diathermy on the Eye, (Abstr.) Am. J. Physiol. **155**: 432 (Dec.) 1948.

6. Mittelmann, E., and Holmquest, H. J.: Useful Power Output of Short Wave Diathermy Apparatus: Determination of Actual Power Absorbed by Patient, Quart. Bull., Northwestern Univ. M. School **14**: 172-182, 1940.

by means of the induction cable, in the form of a pancake, a spiral, or a drum, is preferred in most instances.

Long-wave diathermy provides for a more definite localization of the high-frequency currents than either of the other forms of diathermy. Both the dispersive and active electrodes are metallic and are placed directly

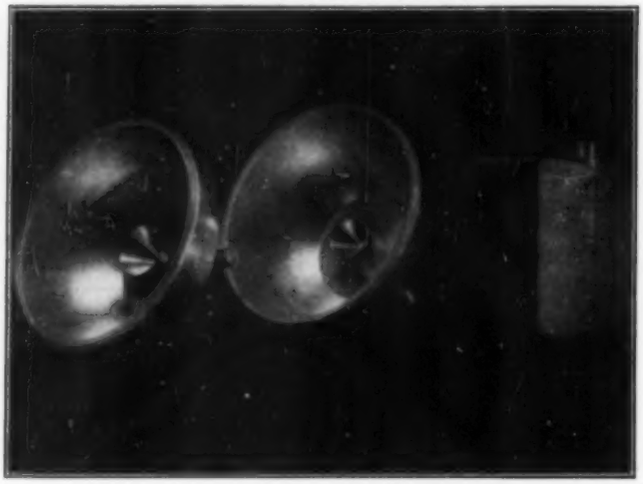

Fig. 1.—Small and large hemispherical and corner type of directors for application of microwave diathermy.

in contact with the skin, and the greatest concentration of heat is developed immediately under the small, or so-called active, electrode.

It is not within the scope of this paper to review the physiologic effects of heat on the tissues. The reader is referred to the specific chapter in the handbook dealing with the physiologic effects of heat for such information.

The source of the electromagnetic radiation that falls in the microwave portion of the spectrum is a multicavity magnetron tube. The high-frequency radiations are conducted from the tube to the director by means of a coaxial cable. The radiations of microwaves have properties somewhat similar to light and infra-red radiation in that they can be reflected, refracted and diffracted. They can also be focused and directed. The apparatus shown in figure 1 uses 3 directors; namely, a hemispherical director 12 cm. in diameter, a hemispherical director 9 cm. in diameter and a so-called corner director. These are used to reflect the radiations of the microwaves from the director usually through a 5 cm. air space, directly onto the tissues to be heated. Areas about 10 inches (25 cm.) in diameter can be covered by the directors available at present. In order to provide controlled or even heating, it is essential that a distance of 5 cm. from director to skin be maintained as accurately as possible. An output of 60 to 80 watts has been used for most of the work for both animals [7] and human beings. The time of application usually varies from twenty to thirty minutes.

The oscillating currents of 10,000 to 100,000 kilocycles (10 to 100 megacycles) used in short-wave diathermy are usually generated in a vacuum tube oscillating circuit by means of 1 or 2 tubes operated on raw or rectified alternating current, which is impressed on the plate circuits of the tubes. At present, in order to conform to the regulations of the Federal Communications Commission, many of the approved apparatuses for diathermic purposes utilize the piezoelectric effect of quartz crystals in their circuits to maintain a constant frequency of oscillation. This property is elicited when a crystal has a voltage applied to it which causes it to change shape; in resuming its original shape, a voltage is generated. This voltage is applied to the grid of the vacuum tubes at a frequency corresponding to the natural resonant frequency of the quartz crystal. Thus the regular rate of vibration of a crystal is used to maintain a constant frequency in the oscillating circuit in the apparatus so that the radiation from the electrodes will conform to the allocated frequencies established by the Federal Communications Commission.

*Methods of Application of Short-wave Diathermy.*—Two general methods of application are used in applying short-wave diathermy. One method employs the electrostatic field provided by pads, cuffs, or air-spaced electrodes. The pads produce superficial heat mainly and are not approved by the Council on Physical Medicine and Rehabilitation. Cuff electrodes are similar to pads, except that they are more suitable for application to extremities and the heat penetrates deeper than when the pads are used. The air-spaced electrodes, which consist of metal electrodes covered with nonconductive material enclosed in a protective cage, have been used more widely than the cuffs or pads. The distance between the electrodes and the surface of the body can be varied easily by adjusting the supporting devices attached to the apparatus.

The other method of general application of short-wave diathermy is conduction of current by means of an insulated cable which is coiled about the part to be treated or enclosed in a case which is a nonconductor and which is either in the form of a disk or in the form of a drum, for greater convenience of application. Use of this method is increasing because of the ease of application and the effectiveness of the induced current in producing desired heating effects in the tissues. It is not necessary to wind the cable around an extremity

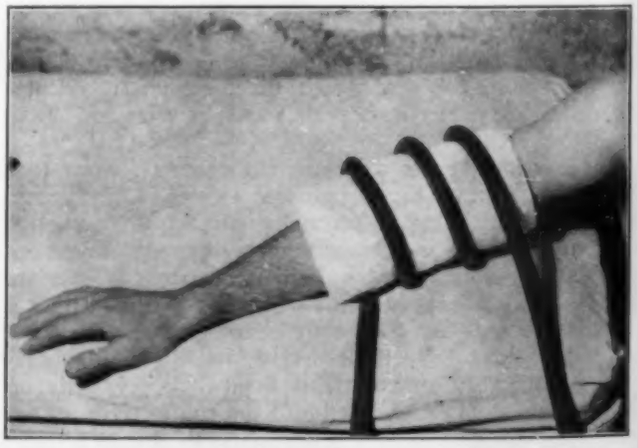

Fig. 2.—Method of applying short-wave diathermy to the elbow by means of an induction coil.

more than 3 or 4 times for effective induction heating (fig. 2). The cable may be coiled to form a pancake for application to flat surfaces (fig. 3). It is always placed over 4 to 6 thicknesses of toweling which will absorb moisture from the surface of the skin and provide a suitable dielectric.

It is important to avoid having metallic objects in the field of radiation in short-wave diathermy because

7. Wise, C. S.; Castleman, Benjamin, and Watkins, A. L.: Effect of Diathermy (Short Wave and Microwave) on Bone Growth in the Albino Rat, J. Bone & Joint Surg. **31**: 487-500 (July) 1949.

of the danger of the metal becoming overheated and burning the adjacent tissues. Extreme caution must be observed if short-wave diathermy is applied to a patient who is lying on an inner spring mattress because of the obvious danger of overheating the springs and causing a fire in the mattress. The time of application

Fig. 3.—Method of applying short-wave diathermy by means of an induction cable arranged in the form of a pancake.

is usually twenty to thirty minutes, and the patient's sensation of heat is used as a guide to intensity of application.

### LONG-WAVE DIATHERMY

Currents used for long-wave diathermy range in frequency from 1,000 to 10,000 kilocycles and are produced by an apparatus which utilizes spark-gap oscillating circuits. The frequencies are variable and many harmonics are present, depending on the width of the spark gaps. Also the forms of the waves are changed by the gaps to produce rough, damped, or smooth, undamped current. Long-wave diathermy is applied by means of metal electrodes in direct contact with the skin. They must be carefully formed and are molded to conform to the contour of the surface to which they are to be applied. Energy is more concentrated beneath the smaller electrode. By varying the size of the electrodes, the concentration of energy may be changed according to the requirements for heating the part being treated. A fairly accurate method of dosage is to administer 50 to 65 milliamperes of current for each square inch of the smaller or active electrode. However, the best guide, as with all heating devices, is the patient's tolerance based on the sensitivity of his skin. Burns are likely to result from contact of the metal electrodes with the uneven surface of the skin.

Long-wave diathermy is also used in surgical procedures. Highly damped waves are used for heating tissues to produce electrocoagulation or electrodesiccation. Undamped current is necessary in order to obtain a cutting current from the apparatus used for surgery. Some apparatuses have a spark-gap generator to produce a damped current for coagulation and a vacuum tube generator to produce the undamped cutting current for cutting.

### APPLICATION OF MEDICAL DIATHERMY

Medical diathermy, in one of its three commonly used forms, provides a useful source of energy for heating the tissues when a local area is to be treated and when a relatively deep or penetrating type of heat is desirable. In many instances when medical diathermy is prescribed, it should be considered as a valuable adjunct to other forms of treatment. It can be prescribed for treatment in many conditions in which it is desirable to obtain one more of the physiologic effects of heat. These have already been described. Studies of the physiologic effects of heat indicate that most patients having conditions that may be benefited by heat will require applications of heat for periods varying from twenty to sixty minutes, one or more times daily.

Some of the commoner conditions which may be benefited by medical diathermy are chronic rheumatoid arthritis, osteo-arthritis, bursitis, tenosynovitis, fibrositis and myositis, sprains and strains, fractures, injuries to tendons, various neuritides (neuralgias and radiculitis), peripheral vascular disease (remote application), acute and chronic sinusitis, otitis media, inflammatory pelvic disease, iritis and uveitis, hematomas, pleurisy and diverticulitis.

*Rheumatoid Arthritis.*—In the treatment of patients having rheumatoid arthritis, medical diathermy has a limited scope of usefulness. It is most valuable when the disease is in the subacute and chronic stages and is useful primarily when only 1 or 2 joints are to be treated. For the patient having rheumatoid arthritis with widespread involvement of many joints, medical diathermy is of little or no value. For rheumatoid arthritis, short-wave diathermy is probably preferable to either microwave or long-wave diathermy, because at the time of our study the latter 2 methods provide heat only in relatively limited areas. Short-wave diathermy can be applied to a single joint (fig. 2), such as an elbow or knee, by means of an induction cable arranged in a spiral coil around the part, with the interposition of a suitable dielectric between the coil and the surface of the joint, or by a drum applicator placed over the part (fig. 4). Short-wave diathermy is usually applied daily for a period of thirty minutes at an intensity determined by the maximal comfortable tolerance of the patient.

*Osteo-arthritis or Hypertrophic Arthritis.*—Short-wave diathermy is useful for treatment of the patient

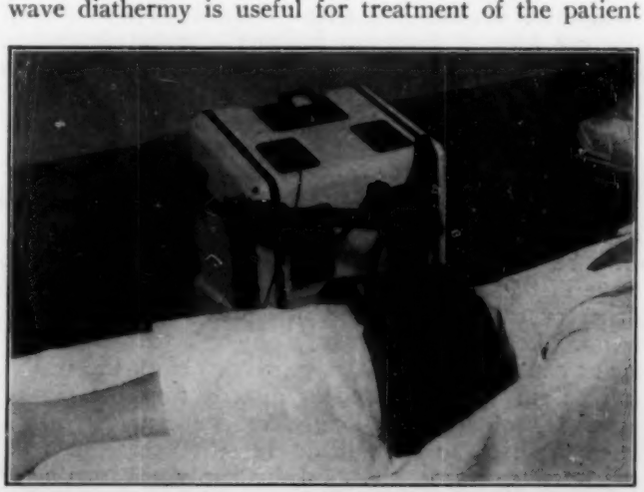

Fig. 4.—Method of applying short-wave diathermy to the knee by means of a hinged type of drum.

having osteo-arthritis of the knees, hips or spinal column. It provides heat which penetrates deeply to the articular tissues as well as to the surrounding muscles and connective tissues. It is of considerable value in providing relief of pain and discomfort related to the muscular spasm that often is associated with osteo-arthritis.

*Bursitis.*—Bursitis involving the subdeltoid, olecranon or ischial bursa is usually considerably relieved in the acute stage by adequate use of diathermy. Any one of the 3 forms of medical diathermy; namely, microwave, short-wave or long-wave, if accurately applied and given in adequate dosage, is a satisfactory method of applying heat. In the acute stage, it may be advisable to apply diathermy two or more times daily for periods of twenty to thirty minutes. Occasionally, in the treatment of patients having acute bursitis, the pain may be aggravated by medical diathermy, especially if the intensity is too high. In these instances, it is advisable to use local applications of cold, or a less penetrating form of heat, such as infra-red radiation. In the subacute and chronic stages, diathermy may be used once or twice daily, followed by massage and exercise to aid in mobilization of the shoulder or elbow. There is some evidence to indicate that the application of diathermy may hasten the absorption of calcareous deposits in the bursa or adjacent tendinous structures. It has not been demonstrated, however, that one form of diathermy has any advantage over the others in this regard. Clinical experience indicates that diathermy with microwaves is an easily applied, comfortable and useful form of treatment for acute and chronic bursitis. Microwave diathermy may be applied with any of the three commonly used directors. The prescription for microwave diathermy may call for exposure for thirty minutes at a distance of 2 inches with an output of 60 to 80 watts (fig. 5). Short-wave diathermy may be applied by means of a hinged drum or cable placed over the area of the involved bursa. Long-wave diathermy can be accurately localized by means of electrodes of molded block tin, which can be cut and shaped to fit directly over the bursal area. The dosage for long-wave diathermy is calculated to be 50 to 65 milliamperes per square inch of the active electrode. Medical diathermy has been used in conjunction with local roentgenoray therapy for bursitis. The combination often proves useful for relieving pain in the acute and early subacute stages of the disease.

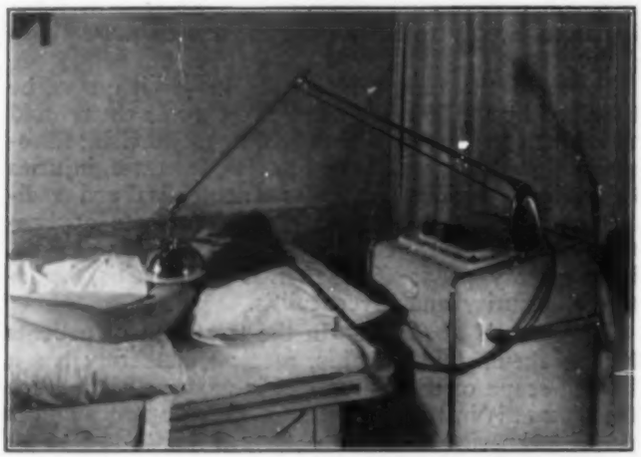

Fig. 5.—Method of applying microwave diathermy to the shoulder by means of a large hemispherical director.

*Tenosynovitis.*—In the treatment of a patient having tenosynovitis in a localized area long-wave diathermy is useful, since it makes possible accurate localization of the heat by means of an electrode of block tin cut and shaped to fit directly over the involved area. Microwave diathermy can be applied best by means of the corner-type or type C applicator. It is important to remember when hemispherical applicators are used for the treatment of a disease localized in a certain area, such as tenosynovitis, that the field of greatest intensity of energy from the microwave is not directly under the center of the director but is approximately 2 inches from the center point. A standard distance of 2 inches from electrode to skin should be accurately measured for all applications of microwave diathermy. Short-wave diathermy, applied either by means of the drum applicator or by the induction cable, can be used in treatment for tenosynovitis. Medical diathermy is applied for thirty minutes, once or twice daily, during the acute and subacute stages.

*Fibrositis and Myositis.*—Patients having muscular pain associated with areas of tenderness and induration in the muscles and supporting tissues are frequently greatly relieved by the application of medical diathermy, which is usually followed by firm massage and exercise. For limited areas of involvement, microwave diathermy may be a satisfactory method of applying heat. Short-wave diathermy, applied by means of the induction cable for thirty minutes, one or two times daily, is useful when a relatively large area may be involved. Long-wave diathermy is of little value in the treatment for fibrositis or myositis.

*Sprains and Strains.*—In cases of sprains or strains in which the ligamentous and capsular structures may be stretched or actually torn, and swelling is present, the use of heat is valuable in hastening the healing and in resolution of the swelling. The application of heat should not be started until the tendency toward hemorrhage is past. Usually this is considered to be within twenty-four to forty-eight hours after the injury. Short-wave diathermy by means of the induction cable is frequently the treatment of choice for a sprain or strain of the knee or ankle. Heat may be applied once or twice daily.

*Fractures.*—Medical diathermy can be used when applications of heat are indicated in the treatment for fractures which have been reduced by closed methods.

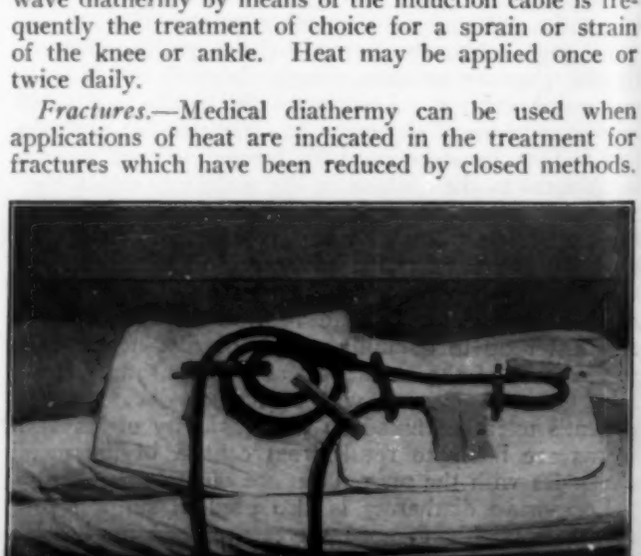

Fig. 6.—Method of applying short-wave diathermy to the lower back and thigh by means of an induction cable arranged in the form of a pancake coil with a loop over the thigh.

In cases in which reduction has been satisfactory and the part well splinted, diathermy can be started several days after the reduction if the part is carefully supported. Diathermy should not be given through a cast, and it should not be used when metallic screws, plates or bands have been used in open reduction. It has not been shown that the use of medical diathermy is superior

to the use of infra-red rays or other forms of heat in the care of fractures after reduction. In diathermy, excessive heating after recent fractures may result in disturbances of growth in the epiphyseal centers of children.

*Neuritis.*—Medical diathermy is often prescribed as part of the treatment of patients having neuritic pains of varying etiology. In the conservative treatment for sciatic pain associated with protruded intervertebral disk, short-wave diathermy is the preferred form of heat. In the acute stage, short-wave diathermy can be applied to the lower back by means of a pancake coil with a single loop extending to the knee or below on the affected side (fig. 6). The heat is usually applied for thirty minutes twice daily. Heat may produce considerable relief of pain in cases of intercostal neuralgias and in some cases of brachial plexus neuritis. In some instances the pain of polyneuritis may be aggravated by medical diathermy. There is danger of causing burns when applying short-wave diathermy to the lower extremities of patients having polyneuritis when circulation is impaired.

*Peripheral Vascular Disease.*—For the patients having an occlusive arterial disease, such as thromboangiitis obliterans or arteriosclerosis obliterans, it may be advisable to apply diathermy or some other form of heat to the upper portion of the thighs or lower portion of the back in an attempt to cause a reflex vasodilatation in the smaller vessels of the extremities which may be in a state of vasoconstriction and not organically occluded. Direct application to the foot and leg is not advised because of the danger of producing burns. Short-wave diathermy may be applied to the sacral area for forty-five minutes once or twice daily with the patient in a warm room and with his extremities covered. Hot moist packs have been considered simple and effective in the application of heat for thrombophlebitis. Usually medical diathermy is not used.

*Sinusitis.*—In cases of acute and chronic sinusitis, medical diathermy is of limited and questionable value. Certainly patients having congested sinuses, tenderness and headache are markedly relieved by the application of heat when drainage is adequate. Diathermy can be applied by means of specially constructed sinus pads that are standard equipment with some machines for short-wave diathermy, or by means of the drum applicator. Until it is possible to protect the eyes adequately, microwave diathermy probably should not be used in the treatment for sinusitis.

*Otitis Media.*—Patients with infections in the middle ear occasionally can obtain considerable relief from pain by the application of heat. Short-wave diathermy can be applied by means of the hinged drum or by having the patient lay on the pancake coil with a suitable dielectric interposed between the coil and the body surface. The time of application should be twenty to thirty minutes once or twice daily.

*Pelvic Inflammatory Disease.*—Medical diathermy can be of considerable value in hastening the resolution of subacute and chronic pelvic inflammations of many patients. Short-wave diathermy can be applied to the pelvic structures by means of a pancake coil placed over the lower portion of the abdomen. Another satisfactory method of hastening resolution is by applying long-wave diathermy to the pelvis by means of a vaginal electrode with an indifferent electrode of block tin applied as a band about the abdomen. Usually considerable resolution will take place with a course of treatment which lasts from ten to fourteen days, heat being applied for one hour twice daily.

*Pleurisy.*—Pain in the wall of the chest which results from pleuritis can be treated satisfactorily with short-wave diathermy by means of the drum applicator or pancake coil placed over the affected area for thirty minutes once or twice daily.

*Diverticulitis.*—In the conservative management of diverticulitis, short-wave diathermy has been used with considerable benefit. It can be applied by placing the pancae coil over the involved portion of the abdomen for thirty to forty-five minutes, twice daily, for a period of one or two weeks.

*Infections of the Eye.*—Short-wave diathermy has proved to be a satisfactory method of applying heat to the eye for certain patients with specific or nonspecific iritis or uveitis. Diathermy may be applied for twenty minutes with the drum applicator twice daily. The application of heat is combined with suitable medication and adequate rest and occasionally with artificial fever therapy. The use of microwave diathermy for treating patients having infectious conditions of the eye has not been completely evaluated at the time of this writing. Until adequate work has been done, microwave diathermy should be considered contraindicated or at least it should be used with extreme caution over the eyes. Experimentally, opacity of the lens has followed exposure of the eye to radiations of microwaves.[4,5]

## CONTRAINDICATIONS TO MEDICAL DIATHERMY

The contraindications to the use of medical diathermy include all of the conditions in which the use of heat in any form is contraindicated. In addition, medical diathermy is contraindicated in a number of specific conditions in which other forms of heat may be useful. Some of the principle dangers of and contraindications to the use of medical diathermy are as follows:

1. *Peripheral Vascular Disease.*—In occlusive arterial disease, such as arteriosclerosis obliterans and thromboangiitis obliterans, in which organic occlusion and ischemia are evident, the local application of diathermy is contraindicated. If the patient has a certain element of vasospasm, the remote application of diathermy or other forms of heat may be permissible and even valuable.

2. *Heat Sensitivity.*—For some patients giving a history of heat sensitivity, a localized application of heat, such as can be obtained with microwave or long-wave diathermy, may be permissible. If syncope or urticaria develop, all heating should be discontinued.

3. *Adhesive Strapping or Moist Dressings.*—Due to the danger of excessive heating of the moisture beneath the adhesive tape or dressing, the application of medical diathermy over these materials is contraindicated. If the adhesive strapping or moist dressings are removed before application of diathermy, a dry dressing can be placed over a draining lesion and changed during the treatment, if necessary, thus permitting the use of medical diathermy.

4. *Hemorrhagic Tendencies.*—In the first twenty-four to forty-eight hours after trauma to the soft tissues, the application of medical diathermy may increase bleeding and the tendency toward swelling in the involved part. Medical diathermy is also contraindicated for patients with purpura or hemophilia. It should not be applied to the back or abdomen of patients who have peptic ulcers which have bled recently.

5. *Metallic Implants.*—In any condition in which metallic implants are present in or near the area to be treated, medical diathermy of any type is contraindicated. Metallic sutures and foreign bodies such as bullets or shrapnel are in the same class as vitallium cups, screws, various types of platings for fractures and metallic bands. It is well known that in many instances damage will not occur. However, there is a potential danger, both actual and theoretical,[8] which makes it advisable to heat these areas by means other than medical diathermy.

6. *Pregnancy.*—The use of diathermy for heating the pelvic and abdominal regions and the lower portion of the back is contraindicated during pregnancy.

7. *Profuse Menstruation.*—Applications of short-wave or long-wave diathermy which utilize a vaginal electrode should be considered contraindicated immediately before or during the menstrual period of patients who give a history of profuse flow. For patients having a scanty menstrual flow, short-wave diathermy usually can be used without deleterious effects. The normal flow for that patient, however, may be increased.

8. *Malignant Disease.*—Medical diathermy is contraindicated in any region where the presence of either primary or metastatic malignant growth is known or suspected.

9. *Osteomyelitis.*—The patient having acute osteomyelitis without adequate drainage or before drainage has been established should not receive medical diathermy.

10. *Effusions and Edema.*—Microwave diathermy should not be used for joints with effusions or highly edematous tissue. Studies of the effects of microwave diathermy on these tissues have not been completed. Based on the factor of the high absorption of energy from microwaves by water and highly fluid mediums, however, this theoretical contraindication should be observed until further information is available.

11. *Transcerebral Application.*—Medical diathermy, used transcerebrally, may cause headache, nausea and vertigo and should be employed with caution. It is usually contraindicated in treatment for most types of headache. It can be used in conjunction with firm massage in an indurative type of headache in which the treatment is applied to the cervical muscles. Treatment over the eyes, frontal sinuses or in the region of the middle ear should be given cautiously, especially if the patient has reported any of the symptoms mentioned.

12. *Anesthetized Areas.*—Heat of any type over anesthetized areas should be used with extreme caution. It is preferable that, if heat is to be employed, an infrared lamp be used which is placed so that the distance from the skin to the source is considerable; the reaction of the skin should be observed constantly. Medical diathermy should be considered contraindicated, or if used, it should be used with extreme caution.

13. *Tuberculosis.*—Medical diathermy is considered contraindicated in the treatment of patients with tuberculosis. If it seems desirable to apply heat to a shoulder or arm of a patient who has active pulmonary lesions a less penetrating form of heat, such as infra-red, should be used. Medical diathermy is contraindicated in the treatment of tuberculous joints.

14. *Thrombophlebitis.*—In the treatment for thrombophlebitis, the use of hot, moist packs has become an accepted procedure. It is possible that short-wave diathermy could be used with a similar effect. Its use, however, has not been accepted generally, and other forms of heat apparently prove adequate.

8. Lion, K. S.: The Effect of the Presence of Metals in Tissues Subjected to Diathermy Treatment, Arch. Phys. Med. **28**: 345-347 (June) 1947.

### SUMMARY AND CONCLUSION

Medical diathermy is one of the most valuable sources of therapeutic heat available to the physician. When a deeply penetrating form of heat is desired, medical diathermy should be considered. If its use seems desirable, the physician should prescribe definitely the type of diathermy he desires, whether it be microwave, short-wave or long-wave. He should prescribe the area to be treated, the type of applicator to be used, the duration of the treatment and the number of treatments desired. Medical diathermy should be prescribed only when it is definitely indicated. The contraindications to its use should be kept in mind constantly, as definite dangers can result from the careless use of medical diathermy. Burns from diathermy may result from faulty technic and are difficult to heal. The use of medical diathermy at home by the patient is a practice which is to be condemned.

If properly employed, medical diathermy can be a most useful form of treatment for many conditions seen in general practice and in many of the medical specialties.

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## Council on Pharmacy and Chemistry

### NEW AND NONOFFICIAL REMEDIES

*The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.*

AUSTIN SMITH, M. D., *Secretary.*

**SPECIAL GELATINE SOLUTION, INTRAVENOUS.—Special Gelatine Solution Intravenous** (KNOX).—A 6 per cent sterile, pyrogen-free, nonantigenic solution of gelatin in physiological sodium chloride for use as an infusion colloid. The gelatine is specially prepared from refined beef bone collagen.

*Actions and Uses.*—Special gelatine solution, intravenous, is specially prepared for injection as a readily available infusion colloid to support blood volume in the management of various types of shock. It is thus used as an osmotically effective substitute for plasma and whole blood when these substances are not otherwise indicated or are not available to meet emergency demands for restoring circulatory volume. In acute or recurrent hemorrhage or shock associated with loss of blood, whole blood is preferable to any other substitute.

Special gelatine solution, intravenous, is largely excreted by the kidney and should therefore not be employed when there is renal impairment; it must be used with care in the presence of cardiac impairment to avoid the undue burden to the circulation of excessive fluid volume. Until further information is available it should not be used in the crush syndrome or in extensive third degree burns because these are associated with possible renal damage.

Since infused gelatine produces pseudoagglutination of the red blood cells that may interfere with typing or cross matching when blood transfusion is to be given later, these tests should be performed before gelatine is used.

*Dosage.*—Special gelatine solution, intravenous, should be warmed to about 50 C. before injection because the solution gels at lower room and refrigerator temperatures. It is completely fluid at body temperatures and must be kept warm for prolonged administration by the drip method. It can be given safely at rates up to 30 cc. per minute. Usually 500 cc. is adequate for a single infusion. About 50 per cent of the gelatine remains in the circulation after 24 hours, so that a single infusion usually gives osmotic protection for 24 to 48 hours.

*Tests and Standards.*—

*Physical Properties:* The gelatine solution is odorless, clear, amber and slightly viscous at temperatures above 29 C., but gels at ordinary room temperature. It has a saline taste due to the added sodium chloride (0.9 per cent). The *p*H of the solution is between 6.95 and 7.40.

Choose a 5 ml. Ostwald pipet with a "water time" of about 1 minute. Calibrate the pipet by determining the time of flow of distiled water at 37 C. Rinse the pipet carefully with gelatine solution, fill with 5 ml. of fresh gelatine solution and place it in a constant-temperature bath at 37 C. After temperature equilibrium has been attained, determine flow time of the gelatine solution. Make three separate time runs and average the time of flow. Calculate the relative viscosity from the equation: relative viscosity = gelatine time (sec.) ÷ water time (sec.). Multiply the relative viscosity by the absolute viscosity of water at 37 C. (6.947 millipoises) to obtain the absolute viscosity of the gelatine solution in millipoises: the absolute viscosity of the gelatine should be not less than 35 nor more than 50 millipoises.

Cut a 15 cm. length of cellophane tubing having a width of about 3 cm. Close one end of the tubing by fitting it over a rubber stopper. Wrap rubber tape tightly over the end of the cellophane tubing to grip it firmly against the rubber stopper. Paint the rubber tape with a water-resistant cement to prevent leakage. Into the other end of the cellophane tube, place a glass tube 20 mm. in diameter and 30 mm. in length which tapers into a 10/30 standard taper female joint. Seal the cellophane to the glass tubing by means of rubber tape and cement as before. Fill the cellophane bag to a mark just below the standard taper joint with gelatine solution previously heated to 37 C. By means of the tapered joint, attach 100 cm. of 4 mm. i.d. glass tubing to the cellophane bag. Place the bag into a 0.9 per cent sodium chloride solution kept at 37 C. Maintain the temperature of the glass tubing which projects beyond the constant-temperature bath as close to 37 C. as possible by placing light bulbs along its length. Allow the solution to rise in the glass tube until no further rise is observed (approximately 48 hours). Measure the distance between the initial and final levels of the solution. Determine the specific gravity of the solution at 37 C. Calculate the osmotic pressure from the equation: O.P. = height of rise (mm.) × [specific gravity of gelatine solution at 37 C. ÷ specific gravity of mercury at 37 C. (13.6)]. The osmotic pressure of the solution is not less than 30 nor more than 60 mm. of mercury.

*Identity Tests:* To 1 ml. of gelatine solution (1:1,000) add 1 ml. of phosphotungstic acid T.S.: a slight precipitate is formed.

To 1 ml. of gelatine solution (1:1,000) add 1 ml. of tannic acid T.S.: the solution becomes turbid immediately.

*Purity Tests:* To 10 Gm. of gelatine solution dissolved in 100 ml. of hot water, add a slight excess of ammonium hydroxide T.S. and 5 ml. of ammonium oxalate T.S.: the precipitate formed on standing overnight should not be greater than that formed in a slightly ammoniacal solution of equal volume containing 0.6 mg. of calcium to which 5 ml. of ammonium oxalate T.S. has been added (0.006 per cent calcium).

Accurately weigh about 10 Gm. of gelatine solution. Transfer it to a 250 ml. Erlenmeyer flask and add 100 ml. of water. Add 1 ml. of saturated potassium chromate solution. Titrate with 0.1 *N* silver nitrate to a slight red endpoint. Each ml. of 0.1 *N* silver nitrate is equivalent to 0.005845 Gm. of sodium chloride: the amount of sodium chloride is not less than 0.85 nor more than 0.95 per cent.

Accurately weigh about 4 Gm. of the gelatine solution in a covered crucible. Place the crucible with cover removed in a drying oven at 125 C. for 1 hour. Cool and weigh. The total solids are not less than 6.7 nor more than 7.1 per cent.

Heat the dried material from the total solids determination over a low Bunsen flame until the organic portion is charred. Add 2 drops of sulfuric acid. Transfer the crucible to a muffle furnace at 600 C. and ash to constant weight. Each Gm. of ash is equivalent to 0.8229 Gm. of ash calculated as sodium chloride. The ash content is not greater than the sum of the percentage of sodium chloride present plus 0.01.

*Assay:* Accurately weigh about 2 Gm. of gelatine solution. Determine the total nitrogen by the semimicro Kjeldahl method *(U.S.P. XIII, p. 672)*. The total nitrogen multiplied by the factor 5.55 is equivalent to the gelatine protein in the sample. The gelatine protein is not less than 5.8 nor more than 6.1 per cent.

KNOX GELATIN PROTEIN PRODUCTS, INC., CAMDEN, N. J.

**Special Gelatin Solution, Intravenous 6%:** 500 cc. bottles. A solution containing 60 mg. of gelatine in each cc.

**PENICILLIN FOR PARENTERAL USE FOR PROLONGED ACTION** (See New and Nonofficial Remedies 1949, p. 153).

The following dosage form has been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

**Aqueous Suspension Rapid/Repository Penicillin:** Crystalline Buffered Potassium/Procaine Penicillin G: 100,000 units/300,000 units in each 1 cc. dose, 1 dose (1 cc.). 5 dose (5 cc.) and 10 dose (10 cc.) vials. The 1 dose size is packaged separately or in combination with 1 cc. ampul of water for injection as diluent.

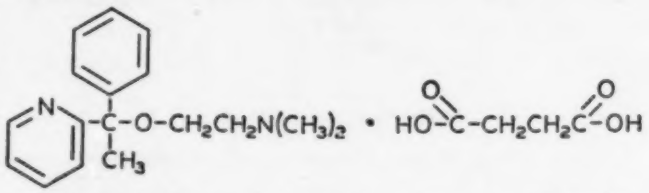
**PROTEIN HYDROLYSATES** (See New and Nonofficial Remedies 1949, p. 413).

The following dosage form has been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

**Solution Aminosol 5% W/W with Dextrose U. S. P. 5% W/W:** 250 cc. infusion solution containers. A modified 5 per cent fibrin hydrolysate with 5 per cent dextrose. Each 100 cc. represents 5 Gm. of protein and 5 Gm. of carbohydrate equivalent to about 40 calories.

**DOXYLAMINE SUCCINATE.—Decapryn Succinate** (MERRELL).—2-[α-(2-Dimethylaminoethoxy)-α-methylbenzyl] pyridine succinate.—$C_{17}H_{22}N_2O.C_4H_6O_4$.—M.W. 388.45.—The structural formula for doxylamine succinate may be represented as follows:



*Actions and Uses*—See general statement on Histamine-Antagonizing Agents. Doxylamine succinate is highly effective in the recommended dose. However, it has a very high index of sedation and in spite of its therapeutic efficacy, its sedative action sometimes precludes its use, particularly where large doses antihistaminics are required.

*Dosage.*—The average adult dose is 25 mg., but the initial dose should be 12.5 mg. and this may be increased until the desired response is obtained or side effects become pronounced.

*Tests and Standards.*—

*Physical Properties:* Doxylamine succinate occurs as a cream to white powder having a characteristic odor. It melts between 100 and 104 C. It is very soluble in water, freely soluble in alcohol and chloroform and slightly soluble in benzene. The free base is obtained as an oil upon the addition of sodium hydroxide T.S. to a 5 per cent solution of doxylamine succinate. A 1 per cent aqueous solution of doxylamine succinate has a pH between 4.9 and 5.1.

*Identity Tests:* Add about 50 mg of doxylamine succinate to 5 ml. of water. To one half of this solution add 2 ml. of a saturated aqueous solution of picric acid: a yellow, gummy precipitate is obtained. To the other half of the solution add several drops of 2 per cent ammonium reineckate: a pink precipitate is obtained. Add about 50 mg. of doxylamine succinate to 1 ml. of sulfuric acid: a clear yellow to light orange solution is obtained, which persists on standing *(differs from diphenhydramine hydrochloride, methapyrilene hydrochloride, pyranisamine maleate, thonzylamine hydrochloride and tripelennamine hydrochloride)*. Dissolve about 0.1 Gm. of doxylamine succinate in 5 ml of water. Add a slight excess of ammonia T.S. and extract the free organic base with ether. Evaporate the aqueous solution to dryness on a steam bath, add about 2 ml. of diluted hydrochloric acid and again evaporate to dryness. Wash the residue with about 10 ml. of ether and evaporate the wash solution to dryness. The white residue melts between 188 and 190 C. *(succinic acid)*.

*Purity Tests:* Dry about 1 Gm. of doxylamine succinate, accurately weighed, in a vacuum desiccator for 5 hours above phosphorus pentoxide: the loss in weight does not exceed 0.5 per cent.

Char about 0.5 Gm. of doxylamine succinate, accurately weighed, over a low flame. Cool, then add 1 ml. of sulfuric acid and continue ignition until no carbon remains: the residue does not exceed 0.1 per cent.

*Assay:* Transfer about 0.4 Gm. of doxylamine succinate, accurately weighed, to a 1 liter volumetric flask and dilute to the mark with distilled water. Mix thoroughly and transfer 10 ml. of the solution to a 100 ml. volumetric flask and dilute to volume with water. The final solution (0.004 per cent) exhibits an ultraviolet absorption maximum at 2600 A ($E^{1\%}_{cm.} = 110 \pm 3$).

Transfer about 0.15 Gm. of doxylamine succinate, accurately weighed, to a semimicro Kjeldahl flask and digest for 3 hours with 7 ml. of sulfuric acid, 2.7 Gm. of potassium sulfate and 0.3 Gm. of mercuric oxide. Cool, add 15 ml. of water, make alkaline with 40 per cent sodium hydroxide and then add 10 ml. of 40 per cent sodium thiosulfate. Distil the ammonia into 20 ml. of 4 per cent boric acid. Using a mixed indicator (1 part of methyl red T.S. and 5 parts of bromocresol green T.S.), titrate the liberated ammonia with 0.05 *N* sulfuric acid. Each ml. of 0.05 *N* sulfuric acid is equivalent to 0.0007004 Gm. of nitrogen: the nitrogen content is not less than 7.00 nor more than 7.30 per cent.

Transfer 0.2 Gm. of doxylamine succinate, accurately weighed, to a 150 ml. beaker and dissolve in 50 ml. of distilled water. Run an electrometric titration with 0.1 *N* sodium hydroxide using a glass electrode. Each ml. of 0.1 *N* sodium hydroxide is equivalent to 0.03885 Gm. of doxylamine succinate: the doxylamine succinate content is not less than 98.5 nor more than 100.5 per cent.

DOXYLAMINE SUCCINATE TABLETS: Crush about 10 tablets and dissolve them in about 25 ml. of water. Filter the solution and to 2 ml. of the filtrate add 1 ml. of a saturated solution of picric acid: a yellow, gummy precipitate is obtained. To a second 2 ml. portion of the filtrate add several drops of 2 per cent ammonium reineckate: a pink precipitate is obtained. To the remainder of the filtrate add a slight excess of ammonia T.S. and extract the solution with ether. Remove the ether by evaporation and add 1 ml. of sulfuric acid to the oily residue: a clear yellow to light orange color is obtained, which persists upon standing.

Powder about 20 tablets, weigh the equivalent of 0.2 Gm. of doxylamine succinate and transfer the powder to a 150 ml. beaker. Proceed as directed in the assay for doxylamine succinate, beginning with ". . . and dissolve in 50 ml. of distilled water." The doxylamine succinate content is not less than 95 nor more than 105 per cent of the claimed amount.

THE WM. S. MERRELL CO., CINCINNATI 15.

**Syrup Decapryn Succinate:** 473 cc. bottles. A syrup containing 1.25 mg. of doxylamine succinate in each cc.

**Tablets Decapryn Succinate:** 12.5 mg. and 25 mg.

U.S. trademark 410,624.

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SATURDAY, JANUARY 7, 1950

## THE NEXT FIFTY YEARS

The advances of medical sciences since the beginning of the twentieth century offer convincing evidence of what can be done when competent researchers can work with freedom, facilities and funds. Never in the recorded medical history of the world have there been so many inspiring discoveries the importance of which has startled at times entire nations. While fundamental discoveries have been made by researchers throughout the world, the practical application of these discoveries, especially during the last two decades, has been effected particularly in the United States. Formerly other countries were regarded highly for their research discoveries and the utilization of research findings, but more recently war and the suppression of personal freedom, among other factors, have intervened so that today researchers from all over the world look expectantly, perhaps even with envy in some instances, toward the Western Hemisphere for its scientific explorations. The research being undertaken elsewhere in the world should not be underestimated and should be encouraged. However, unquestionably it is not as productive as it would have been if catastrophic influences had not intervened.

A review of the medical discoveries since the turn of the century provides so many revelations that books could be and have been written of the importance of these findings. Drugs and operations, for example, alone can provide endless material for stories of the onward march of the medical researchers. Insulin, vitamins, sulfonamides and penicillin are only a few of the outstanding discoveries in the drug field. Operations formerly undreamed of are now everyday occurrences. Isotopes and betatrons have become part of the medical language. Ideas now only in the stage of laboratory development are in some instances truly startling. Even entirely new approaches to illnesses have been conceived, as the result of which the full possibilities of formerly practically unknown subjects, such as physical medicine and rehabilitation, are being explored with a thoroughness that offers much promise for the future. Truly the past fifty years have been remarkable for those who devote their lives to the prevention of illness and the treatment of the sick.

One of the frequently overlooked aspects of these modern medical miracles is the recentness of many discoveries and the speed with which these discoveries were put into practical use. Insulin sounds like an old name, but it was discovered in the early twenties. The sulfonamides have been in general use only two or three years more than a decade. The widespread use of penicillin is less than ten years old. Only a comparatively short time ago these and other drugs were at best research dreams. Yet today they are available in almost inconceivable amounts and have changed completely the control of many diseases. Some diseases have almost been eradicated; at least they do not constitute serious health hazards. Other diseases are being brought under control at such frequent intervals that many persons have not grasped the enormity of such medical efforts. They accept these advances as commonplace.

The discovery, introduction and general acceptance of any new technic generally are based on much hard work and the expenditure of countless hours of trial and disappointment. Seldom is a great discovery made by chance; an observation may be based on good fortune, but it is not by chance that the observer was trained to recognize the significance of his observation. Nor is the development of industrial resources to make available a new drug based on luck. The story of the manufacture of penicillin from its early days to the present is filled with evidence of what is required before a new drug is ready for general acceptance.

And so it is with other discoveries. Only by careful trial, retention of the desirable features and rejection of the undesirable, is it possible to offer something of merit. This development does not stem from a single effort but from a succession of research projects in which many researchers with varied interests participate. The educational backgrounds, the practical training and individual research interests are varied but necessary. Without such varied resources progress would be much slower. One of the significant factors in medical research is the great variation in individual makeup of the researcher. Some researchers are plodding. Others are volatile and explosive. Some work best alone. Others seem to thrive on companionship. Some pursue relentlessly a single idea and persistently explore minute details. Others are content to leave detailed work for assistants. Some are trained as clinicians, some in other fields. Representatives of all races and creeds can be found working side by side. In the interest of health, personal political inclinations should not be important in research environments if the latter are to be kept free of political interference or domination.

Thus it has been possible in some countries to search successfully for answers to health problems, while in other countries the research explorations are hampered constantly by various influences. Time after time in some countries lack of understanding and even selfish interests have interfered with the efforts of researchers to seek new treatments or explore new paths leading to new treatments. In some instances research has been by government decree. The results have shown the fallacy of such direction of effort. In the United States today it is still possible to engage in research without political interference, although from time to time there are attempts to introduce measures which would remove in time all barriers to the political control of research and its participants. Because of the present freedom, physicians learn almost daily, it seems, of new treatments, and patients receive the benefits of these medical advances as soon as their value is determined satisfactorily. Because of this freedom, researchers from all over the world are seeking opportunities to work in the laboratories and clinics in this country so that they may learn the latest treatments and observe the latest research technics. Fortunately these observers are being welcomed in increasing numbers. They provide an invaluable source for the dissemination of information on health, which can be of tremendous importance in the establishment of world peace. A healthy nation is more likely to be a happy nation. The possible contributions to international understanding and contentment that can be made by medical and allied researchers are too important to be ignored.

While many diseases have been brought under control in the past fifty years, these advances probably will be overshadowed by the events that certainly will occur in the next fifty years. In the year 2000 A.D., new treatments, new preventive measures and new diagnostic procedures will render obsolete some of our present approaches to health problems. Many of the diseases not now susceptible to satisfactory medical control unquestionably will be treated successfully or prevented. It is hoped that cancer, anterior poliomyelitis, arthritis, degenerative diseases and some diseases of the central nervous system will be in the list of diseases conquered in the comparatively near future. However, such achievements will require cooperation, patience, understanding and constant vigilance to protect the unwary from deception, to shield the naive from beguiling temptations offered by those whose sole interest is the satisfaction of personal ambition, and to expose that which is medically wrong for the people of any nation. Physicians and others have fought for medical advancements, and the medical advances that have been made in the past fifty years are of immeasurable importance to the world. We enter 1950 with the hope that the advances of the past half-century will be far overshadowed by those in the coming half-century. The future looks promising if we meet all our responsibilities as clinicians, teachers, researchers and citizens. This will require ceaseless efforts as individuals and as members of scientific organizations.

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## LOBOTOMY FOR RELIEF OF PAIN

In 1946 Watts and Freeman [1] reported on a small group of patients in whom intractable pain was relieved by bilateral prefrontal lobotomy. In this group there were 6 patients with mental disorders in whom the predominant symptom was unbearable pain and 3 patients with severe intractable pain due to organic disease. These authors stressed the distinction between perception of pain and reaction to pain. Perception of pain may be evaluated in terms of quality, intensity and temporal aspects, whereas reaction to pain is manifested by such symptoms as tachycardia, panting, bowel disturbances, anxiety, fear, terror, panic and prostration. Psychosurgery alters the patient's reactions to pain without materially changing his ability to feel the pain.

Scarff [2] performed a unilateral prefrontal lobotomy on 33 patients for the relief of pain. The patients were studied for periods ranging from one month to ten months following operation. The unilateral procedure is said to present the advantage over the bilateral because it does not adversely affect the intellect and the personality of the patient. The results obtained were apparently as satisfactory as those obtained by Watts and Freeman with bilateral lobotomy. Scarff at the same time observed that abrupt termination of the use of narcotics, on which some of these patients had become dependent for the relief of pain prior to operation, was not followed postoperatively by any of the usual withdrawal symptoms. The result in 22 of the 33 patients was considered definitely satisfactory or good. The preoperative pain in these patients was due to a variety of pathologic processes, such as carcinoma of the tongue, carcinoma of the jaw, trigeminal neuralgia, aneurysm of the thoracic aorta, carcinoma of the pancreas, metastatic carcinoma of long bones, metastases to the spine and advanced arthritis. The results in 22, or 66 per cent of the series, are claimed to have been completely satisfactory; the patients were followed for an average of two and one-half months. In 5 patients, or 15 per cent of the series, the results were unsatisfactory. In 3 patients of the group with poor results immediate relief of pain was later followed

1. Watts, J. W., and Freeman, W.: Psychosurgery for the Relief of Unbearable Pain, J. Internat. Coll. Surgeons **9**: 679 (Nov.-Dec.) 1946.
2. Scarff, J. E.: Unilateral Prefrontal Lobotomy for the Relief of Intractable Pain and Termination of Narcotic Addiction, Surg., Gynec. & Obst. **89**: 385 (Oct.) 1949.

by return of pain. The failure of unilateral prefrontal lobotomy in these patients, Scarff believes, may be explained by the assumption that the operation introduces a quantitative rather than an absolute barrier to the experience of pain and that, if pain increases sufficiently, it may penetrate this barrier to some degree. The impression entertained by him at an earlier date that the site of the operation was a factor was not supported by later observations. There was no evidence in this group of patients establishing the superiority of the ipsilateral lobotomy or of lobotomy on the dominant hemisphere. Scarff stresses that, if pain is to be relieved by unilateral lobotomy, the lobotomy must be thorough and this can be accomplished only under direct vision. The operation does not cause much shock and therefore may be employed advantageously in persons who could not tolerate more difficult technical procedures, such as high cervical chordotomy, medullary tractotomy, section of multiple cranial nerves or mesencephalic tractotomy.

Psychometric evaluations of 15 patients of this group performed before and after operation and of postoperative evaluations in 9 other paients did not reveal significant alteration in intellect or personality. An unforeseen effect of the unilateral lobotomy was the absence of withdrawal symptoms in 15 patients who were addicted to the use of drugs for the relief of pain.

The results, as reported by Watts and Freeman and by Scarff, suggest that relief of intractable pain in many conditions may be accomplished by a bilateral or unilateral prefrontal lobotomy. However, since the technic still is in need of further study, it should not be employed carelessly. The operation is best reserved for carefully selected patients and should be performed only by persons who are experienced in its use, otherwise, abuse may arise before all phases have been explored and the operation then may be cast aside as not suited to medical practice.

## Current Comment

### NAME OF HYGEIA TO BE CHANGED TO TODAY'S HEALTH

With the March 1950 issue, *Hygeia* will be known as *Today's Health*. This periodical, which has been issued on a monthly basis since its inception in 1923, has become widely known as the "health magazine of the American Medical Association." At its November 5 meeting the Board of Trustees voted to adopt a title which better reflects the subject matter of this journal. Dr. W. W. Bauer, director of the Bureau of Health Education, who has been associate editor of *Hygeia* since 1932, has been named editor to succeed Dr. Morris Fishbein, who has resigned this position. Dr. W. W. Bolton, associate director of the Bureau of Health Education, has been named associate editor of *Today's Health*. Mr. Ellwood Douglas will continue as managing editor.

### TENTH ANNUAL CONGRESS ON INDUSTRIAL HEALTH

The Tenth Annual Congress on Industrial Health will be held at the Roosevelt Hotel in New York City on Monday and Tuesday, Feb. 20 and 21, 1950, under the sponsorship of the Council on Industrial Health of the American Medical Association and the Medical Society of the State of New York. At the opening session the Council will report briefly on progress made in industrial health during the past ten years and will define some goals for the next decade. The director of the recently created Commission on Chronic Illness will discuss the importance of this development to industrial management and workers. The Committee on Advancement of Health in Industry created at the last congress and jointly sponsored by the Council on Industrial Health and the Division of Industrial Hygiene of the Public Health Service will present a résumé of its major findings. Since continued interest in civil defense is essential, several speakers will discuss this topic. If disaster occurs industry must be prepared for it. On the afternoon of the first day a panel of experts on medical care of workers will discuss the variations in four major types of plans: (1) union plans, (2) management plans, (3) private insurance plans and (4) medical society and Blue Cross plans. After the discussions, written questions from the audience will be answered by the panel members. On Monday evening the Council on Industrial Health will entertain the official representatives of state medical societies at its Annual States' Relations Dinner. Others are welcome to attend and may secure tickets at the registration desk on the opening day of the congress. Tuesday morning will be devoted to a discussion of relations among the medical, engineering and social sciences. Problems of production and human relations and the aging worker will be stressed. The first of two symposiums on Tuesday afternoon is concerned with the experience of a large corporation in the development of new technics for the selection, placement and follow-up of employees. This will be a practical demonstration of the aids now required to cope successfully with the hiring and maintenance in employment of workers. The other symposium will review the essential elements of case-finding programs in industry and will demonstrate how early diagnosis can be improved and extended, which is particularly advantageous to the small plant in the small community. Several technical committees appointed by the Council will hold working sessions during the congress. Subjects to be discussed will be noise in industry and economic poisons. Attendance at these working conferences must necessarily be limited to members and invited guests. Those especially interested may secure further details from the office of the Council on Industrial Health, American Medical Association, 535 North Dearborn Street, Chicago 10.

# ORGANIZATION SECTION

## Official Notes

### SPECIAL FEATURES—SCIENTIFIC EXHIBIT SAN FRANCISCO SESSION

The Committee on Scientific Exhibit is arranging several special features for the San Francisco Session. The special exhibit on fractures will be presented again under the auspices of a committee consisting of Dr. Kellogg Speed, Chicago, chairman; Dr. Gordon M. Morrison, Boston, and Dr. Frederick A. Jostes, St. Louis.

There will be a group of exhibits on diseases of the Pacific area arranged in cooperation with the American Society for Tropical Medicine and the American Foundation for Tropical Medicine.

An outstanding program of motion pictures will be shown with the assistance of the Committee on Medical Motion Pictures, the films being carefully chosen for their suitability and value to the practicing physician.

Each of the nineteen sections of the Scientific Assembly will be represented by groups of exhibits dealing with the various branches of medicine. Applications for space in the Scientific Exhibit and for time on the motion picture program close on January 30. Application blanks may be obtained from the Section representatives or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10.

## Washington Letter

*(From a Special Correspondent)*

Jan. 3, 1950.

### Estimate of Number of Physicians Required

Just published by the U. S. Public Health Service is a monograph which estimates the country's future requirements of general practitioners and specialists. Its many tables and figures, dealing with prewar distribution of physicians as well as estimated needs in the year 1960, comprise a statistical work that promises to have value for reference purposes, particularly with respect to pending congressional legislation on medical care and public health.

The year 1940 was selected as a base for the study since it was the latest year for which complete census data were available and the American Medical Directory for that year was the most recent source of figures on geographic distribution which did not reflect dislocations incidental to mobilization. Dr. Donald G. Anderson, secretary of the Council on Medical Education and Hospitals, American Medical Association, and Frank G. Dickinson (Ph.D.), director of the Bureau of Medical Economic Research, assisted in preparation of the monograph, the authors of which are Dr. Joseph W. Mountin, assistant Surgeon General, and Elliott H. Pennell and Anne G. Berger, statisticians, of the Bureau of State Services, U. S. Public Health Service.

Largely on the basis of figures supplied by the American Medical Association, the report estimates the present number of licensed physicians at 202,516, or 137 per 100,000 population. One fourth of the total are classified as specialists, compared with 11 per cent in 1923. The number of physicians engaged in "rendering medical services directly to the civilian population" is reckoned at 160,480, of whom 124,404 are general practitioners and the remainder specialists.

On the assumption that the country's population in 1960 will be 158,000,000, a minimum of 244,000 physicians would be required, according to the study. The forecast of supply in 1960 is 227,000. On the other hand, an oversupply of specialists is in prospect in all categories, with the exception of tuberculosis.

### Shielding Requirements Against Radiation Determined

An investigation by National Bureau of Standards engineers has resulted in determination of shielding requirements for adequate protection of workers from gamma rays emitted by cobalt 60, which is being employed in increasing amounts in treatment of cancer and animal nutrition studies. The study concluded that concrete is an effective protective barrier for storage vaults and other stationary installations.

Known as Public Health Bulletin No. 305, the monograph is purchasable (45 cents) from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. It is anticipated that comments on the publication will be forthcoming from the Council on Medical Education and Hospitals. Incidentally, a prefactory note acknowledging assistance rendered by Dr. Anderson and Dr. Dickinson makes it clear that their endorsement of the report's figures is not implied and that the authors alone are responsible for the working hypotheses, statistical procedures and results presented.

### Study Depicts Loneliness of VA Mental Patients

A survey conducted by the psychiatry and neurology division of Veterans Administration discloses that one third of the 52,000 mental patients in VA hospitals have been visited by neither family nor friends for a year or more. In one hospital only 219 of 785 patients had had a visitor in the previous year. Dr. Harvey J. Tompkins, chief of the psychiatry and neurology division, stated that while visitors might be disturbing in some instances, they would be highly beneficial to the patients in the majority of cases. The survey uncovered numerous cases of "forgotten veterans," whose families wanted to have nothing to do with them and who prolonged the patients' hospitalization because they refused to accept them back home when medical discharge was indicated.

### Veterans Medical Department Sets up New Unit

Veterans Administration has announced establishment of a new field operations service in the Department of Medicine and Surgery, to be headed by Dr. Robert C. Cook, formerly deputy medical director. Since November 1947, Dr. Cook has been manager of the veterans hospital at Fort Logan, Colo. The new unit will be composed of three divisions: Field Liaison, Hospital Administration, and Hospital Requirements and Equipment. Dr. Cook will serve at Washington headquarters as chief officer for all matters involving over-all operations of veterans hospitals. A veteran of World Wars I and II, Dr. Cook is a member of the Denver City and County Medical Society, Association of Military Surgeons and American Medical Association.

## Coming Medical Meetings

Annual Congress on Medical Education and Licensure, Chicago, Palmer House, Feb. 5-7. Dr. Donald G. Anderson, 535 N. Dearborn. St., Chicago, Secretary.

National Conference on Rural Health, Kansas City, Mo. Feb. 3-4. Dr. F. S. Crockett, 535 N. Dearborn St., Chicago, Chairman.

American Academy of Orthopedic Surgeons, New York, Waldorf-Astoria Hotel, Feb. 11-16. Dr. Harold B. Boyd, 869 Madison Ave., Memphis, Tenn., Secretary.

# GOVERNMENT SERVICES

## NAVY

### COURSE FOR RESERVE OFFICERS

The Bureau of Medicine and Surgery will conduct a course of instruction in medical aspects of special weapons and radioactive isotopes at the Naval Medical School, Bethesda, Md., January 23-27. This course is being conducted primarily for the benefit of inactive reserve medical and dental officers and will present the problems likely to be confronted and technics to be employed in the field of radioactivity. The speakers will be outstanding men in their specialties. Inactive reserve medical and dental officers who desire to attend this course should submit a request for training duty at the earliest possible date to the commandant of their local naval district. Facilities available at the Naval Medical School make it necessary to restrict attendance to 200 reserve medical and dental officers.

### SELECT 187 SENIOR STUDENTS FOR INTERN TRAINING

A total of 187 senior students who will graduate from civilian medical schools throughout the country in 1950 have been selected to serve their internship in U. S. Navy hospitals under the Navy's graduate medical training program, Rear Admiral C. A. Swanson, Surgeon General of the Navy, announced. The students will be appointed lieutenants (junior grade) in the Medical Corps, Naval Reserve, on graduation and will be ordered to active duty at a naval hospital approved by the American Medical Association's Council on Medical Education and Hospitals.

### PERSONAL

Capt. Richard H. Fletcher (MC), U. S. Navy, head of the Training Branch, Professional Division, Bureau of Medicine and Surgery, has been appointed a member of the Council on Education of the American Hospital Association.

### GRADUATE TRAINING

The following medical officers have been nominated for residency training under the Graduate Training Program:

Comdr. George N. Schiff, to a residency in obstetrics and gynecology, Naval Hospital, Great Lakes, Ill.

Comdr. Joseph A. Syslo, to a residency in urology, Naval Hospital, St. Albans, L. I., N. Y.

Lieut. Comdr. William J. Hall, to a residency in surgery, Naval Hospital, St. Albans, L. I., N. Y.

Lieut. Comdr. Clyde W. Norman, to a residency in general practice, Naval Hospital, Long Beach, Calif.

Lieut. (jg) Morton Johan, to a residency in psychiatry, Naval Hospital, Bethesda, Md.

Comdr. John H. Cox, to a residency in dermatology and syphilology, Naval Hospital, Philadelphia.

Comdr. Miles C. Krepela, to a residency in children's orthopedics, James W. Riley Memorial Hospital, Indiana University, Indianapolis.

Comdr. Clifford A. Stevenson, to a fellowship in children's orthopedics, University of Oklahoma Hospitals, Oklahoma City.

Lieut. Comdr. Joseph R. Connelly, to a fellowship in plastic surgery at various Memphis hospitals on the plastic surgery service of Dr. Wm. M. Adams, Memphis, Tenn.

Lieut. Alvis B. Dickson, to a fellowship in children's orthopedics, Alfred I. DuMont Institute, Wilmington, Del.

Lieut. James A. Kaufman, to a residency in surgery, Naval Hospital, Philadelphia.

Lieut. (jg) Harold M. Peacock, to a residency in surgery, Naval Hospital, Long Beach, Calif.

### RESERVE OFFICERS REQUEST ACTIVE DUTY

The following reserve medical officers have requested active duty and have been assigned as follows:

Lieut. (jg) Joseph H. Batsche, of Cincinnati, to the Naval Air Station, Corpus Christi, Texas.

Lieut. (jg) Edward W. Bird, of Santa Barbara, Calif., to the Naval Hospital, Long Beach, Calif.

Lieut. (jg) William E. Fraser, of Scarsdale, N. Y., to the Naval Auxiliary Air Station, Charlestown, R. I.

Lieut. (jg) Thomas J. Anderson, of Greensboro, Ala., to the Naval Hospital, Philadelphia.

Lieut. (jg) Ned H. Wiebenga, of Lawrence, Mass., to the Naval Hospital, Great Lakes, Ill.

Lieut. (jg) William N. Young, of Chelsea, Mass., to the Naval Hospital, Great Lakes, Ill.

## AIR FORCE

### CIVILIAN INTERN PROGRAM

The U. S. Air Force Medical Service will commission 200 selected civilian interns in the Air Force Reserve as first lieutenants on active duty with full pay and allowances, according to an announcement by Major Gen. Harry G. Armstrong, the Surgeon General. Eligible to receive commissions are physicians who will be graduated from approved medical schools between Jan. 1 and July 1, 1950, and who are to begin internships between those dates in approved civilian hospitals. Physicians who are so commissioned will serve two years of active duty for each year of internship as commissioned Air Force Reserve officers at Air Force medical installations. Information concerning the intern program may be obtained on request to deans of medical schools or the Officer's Procurement Branch, Office of the Surgeon General, Headquarters, U. S. Air Force, Washington 25, D. C.

### PERSONAL

Brigadier Gen. William H. Powell Jr., director, Professional Services, U. S. Air Force, Surgeon General's Office, addressed the graduating flight nurses at the School of Aviation Medicine, Randolph Air Force Base, Texas, Dec. 8, 1949. In addition to the Air Force graduates were 10 Navy nurses and 5 Medical Service Corps officers.

## SECRETARY OF DEFENSE

### SPECIAL MEETING OF EPIDEMIOLOGIC BOARD

A special meeting of the Armed Forces Epidemiological Board was held November 30 at the Army Medical Center, Washington, D. C. Established by the Secretary of War in January 1941 as the Army Epidemiological Board, it was reconstituted recently by the Secretary of Defense as the Armed Forces Epidemiological Board, to meet the needs of the three services. The board acts as an advisory body to the surgeons general of the Army, Navy and Air Force on the scientific aspects of diseases and their control. The board is composed of nine civilians: Drs. Colin M. MacLeod, professor in the College of Medicine, New York University; Francis G. Blake, Yale University School of Medicine; Lowell T. Coggeshall, Division of Biological Sciences, University of Chicago; R. E. Dyer, National Institutes of Health; I. S. Ravdin, University Hospital, Philadelphia; Thomas M. Rivers, Hospital of the Rockefeller Institute for Medical Research; James S. Simmons, School of Public Health, Harvard University; W. Barry Wood, Washington University, St. Louis, and Ernest L. Stebbins, School of Hygiene and Public Health, Johns Hopkins University.

# PUBLIC HEALTH SERVICE

## THE LOWEST DEATH RATE

The crude death rate for 1948 was 9.9 per 1,000 population, the lowest in the history of the country. The 1948 rate, which was just announced, was 2 per cent below the rate of 10.1 for 1947 and 1 per cent lower than the 1946 rate, the previous record low. The major chronic diseases associated with advanced age accounted for 63 of every 100 deaths. The death rate in this group showed only slight changes from 1947. The number of deaths from poliomyelitis and acute polioencephalitis rose from 580 deaths in 1947 to 1,895 in 1948 and brought the death rate back up to the 1946 level of 1.3 per 100,000 population. Deaths from measles rose from 472 in 1947 to 888 in 1948 but remained under the 1946 total of 1,310. The leading causes of death remained the same as in 1947: diseases of the heart, malignant tumors, intracranial lesions of vascular origin, nephritis, accidents (excluding motor vehicle), pneumonia and influenza, tuberculosis, premature birth, diabetes mellitus and motor vehicle accidents.

## SAN DIEGO X-RAY SURVEY

The San Diego Metropolitan Mass Chest X-Ray Survey team broke all previous mass survey records when 52,391 persons were thus examined during the first five days of operation. A public health service team under the direction of Dr. LeRoy Allen is working with state and local agencies during the survey. The survey is offering free roentgenograms at 19 portable and mobile x-ray units placed in strategic spots around San Diego. The San Diego Metropolitan Mass Chest X-Ray Survey is sponsored by the California State Department of Public Health, San Diego County Medical Society, San Diego County Tuberculosis and Health Association, Departments of Public Health of the City and County of San Diego and the U. S. Public Health Service.

## RADIOLOGIC HEALTH PROGRAM

Formation of a new unit under the Public Health Service, to develop a radiologic health program to meet potential health hazards created by increased use of radioactive materials and radiation-producing machinery, has been announced. The new unit is under the direction of Dr. Edwin G. Williams, a Public Health Service medical director. The Radiological Health Branch will correlate radiologic health activities in the Public Health Service, develop a training program in radiologic health for service officers and other public health workers and act as a source of information on radiologic health for other units of the service, for other federal agencies and for state and local health agencies. Surgeon General Leonard A. Scheele said that radioactive materials in use include radium and radioactive isotopes, such as radioiodine, radioiron, radiophosphorus and radiosodium. Radiation-producing machines, he said, include x-rays, fluoroscopes, cyclotrons, betatrons and other atomic-particle accelerators.

## MORE FEDERAL FUNDS FOR RESEARCH

Public Health Service grants totaling $835,770 for medical research projects at nonfederal institutions were announced Dec. 4, 1949 by the Federal Security Administrator. A total of 105 projects will be supported at 61 institutions located in 29 states, the District of Columbia and three foreign countries. The projects are designed to provide new scientific data on a wide variety of human ailments. They include studies of the effect of parental age on longevity, the use of streptomycin in tuberculosis, the electrical activity of the central nervous system and the psychosomatic aspects of peptic ulcer. These are in addition to grants announced in August, amounting to $2,056,426.

The projects also include studies of the effect of ultrasonic vibrations (i. e., sounds that are above the limit of human hearing) on bacteria and suspended particles in polluted waters, physiologic criteria for the evaluation of the mode of action of insecticides and the strains of influenza virus involved in the European epidemic of last winter.

## THE ASHFORD AWARD

Dr. Robert J. Huebner, chief, Virus and Rickettsial Section, National Institutes of Health, is recipient of the Bailey K. Ashford Award for his research on rickettsialpox and Q fever. The Virus and Rickettsial Section is in the Laboratory of Infectious Diseases of the Microbiological Institute. The award, which is made every two years to a scientist under 35 who has contributed most to research in tropical medicine, was presented Dr. Huebner at the recent joint annual meeting of the American Society of Tropical Medicine, the American Academy of Tropical Medicine and the National Malaria Society.

# MISCELLANEOUS

## PROVISIONS FOR OPERATION OF FELLOWSHIP PROGRAM

The U. S. Atomic Energy Commission announces the provisions under which the fellowship program will be administered by the National Research Council during the 1950-1951 academic year. New predoctoral fellowships will not be offered. The commission plans to explore further the desirability of sponsoring a predoctoral fellowship program in fields relating to atomic energy and intends to seek the advice of the National Academy of Sciences.

New postdoctoral fellowships in the physical sciences, biology, biophysics and medicine will be offered only for advanced training in fields of research closely related to the national atomic energy program wherein access to secret data is required or desirable. New postdoctoral fellowships will not be awarded until applicants have been investigated as to character, associations and loyalty by the Federal Bureau of Investigation and granted full security clearance by the AEC for access to "restricted data."

To fulfil previous commitments, applications for renewal of current nonsecret predoctoral fellowships and postdoctoral medical fellowships will be accepted. Such renewals, however, will be granted only to applicants who have been investigated by the FBI and granted "fellowship approval" as to loyalty by the AEC.

Under the program set up for next year, it is expected that about 75 new awards will be offered and about 175 renewals of current fellowships granted.

At present there are 421 AEC fellows. Of these, 30 are engaged in research requiring access to secret data and have therefore been granted full security clearance. Of the 391 engaged in nonsecret work, 77 were appointed or reappointed after August 24, when the 1950 Appropriations Act took effect, and therefore have been investigated and granted fellowship approval as to loyalty, and 314 were appointed before August 24 and therefore have been required only to sign the loyalty oath and non-Communist affidavit required of all fellows since May 22.

The AEC also announced that the fellowship in health physics, formerly a part of the NRC-administered predoctoral program, now discontinued, will be continued in the next academic year, although they will not be administered by the NRC. Fellowship awards in health physics, of which there will be about 20 next year, will continue to be conditioned on FBI investigation and full security clearance by the AEC, as they have been in the past.

The actions announced do not affect the research being carried on at the AEC's three national laboratories by graduate students, of whom there are 15 using the facilities of the Brookhaven National Laboratory, 10 at the Argonne National Laboratory and 7 at Oak Ridge.

# Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

## ALABAMA

**Portrait of Dr. McLester.**—A portrait of Dr. James S. McLester, professor emeritus of medicine at the University of Alabama College of Medicine, University, will be unveiled at the College Auditorium on January 15. This portrait will be formally presented to the college by the residents and former residents who have served under Dr. McLester in the department of medicine, as a token of appreciation for his long years of service.

**Mental Hygiene Clinic.**—The Tuscaloosa Mental Hygiene Clinic has been opened as the second such clinic in the state program. It will serve Tuscaloosa and the surrounding towns and counties. The hours are 1 to 5 p. m. Monday through Friday. The clinic, sponsored by the Mental Hygiene Division of the state department of health, will aim to prevent serious mental illness by early detection, diagnosis and treatment of personality maladjustments.

## ARKANSAS

**Neuropsychiatric Meeting.**—The annual Neuropsychiatric Meeting at the Veterans Administration Hospital, North Little Rock, will be held on February 23-24. A number of nationally known leaders in neuropsychiatry and related fields are expected to participate, including Drs. Walter C. Alvarez, Rochester, Minn.; Daniel Blain and Pearce Bailey, Washington, D. C.; Edwin E. Gildea, St. Louis; Karl A. Menninger, Topeka, Kan., and Howard Rusk and John N. Rosen, New York. There will be no charge for registration. All interested professional personnel are welcome to attend. Information may be obtained by writing to the Director of Professional Education, Veterans Administration Hospital, North Little Rock.

## ILLINOIS

**Televise Hobbies for Health.**—A televised Health Talk over WGN-TV January 11 will emphasize the importance of hobbies for health. The telecast, which is sponsored by the Educational Committee of the Illinois State Medical Society in cooperation with WGN-TV in a regular weekly series, will feature the following Chicago physicians and their hobbies: Walter S. Priest, viola; Otto Saphir, cello; William A. Brams and Louis Krasno, violins; Benjamin Rappaport, painting; William C. Buchbinder, piano; Leo M. Zimmerman, woodcarving, and Harold M. Camp, fishing. Dr. Andy Hall, of Mount Vernon, who recently won the general practitioner award of the American Medical Association, will be interviewed.

### Chicago

**Phi Lambda Kappa Lecture.**—The Alpha Alpha Chapter of the Phi Lambda Kappa medical fraternity will hold its second annual lecture January 18 at 1 p. m. in room 221 at the University of Illinois College of Medicine. Professor William C. Rose, Ph.D., head of the department of biochemistry at the University of Illinois, Urbana, will speak on "The Role of the Amino Acids in Nutrition."

**Institute of Medicine Election.**—At the annual meeting of the Board of Governors of the Institute of Medicine of Chicago, December 12, the following officers were elected for 1950: Drs. Henry T. Ricketts, chairman of the Board of Governors; Stanley Gibson, president; Otto F. Kampmeier, vice president; George H. Coleman, secretary, and E. Lee Strohl, treasurer. Newly elected members of the Board of Governors are Drs. Leon Bloch, E. Lee Strohl, and Allan G. Brodie, D.D.S.

**Lectures for Alumni.**—The Chicago Medical School will present a series of graduate lectures for its alumni in the Kling Auditorium of Mount Sinai Hospital Wednesday evenings beginning January 11 at 8 p. m. The subjects will consist essentially of the newer advances in medicine. A partial list of topics to be covered include: ACTH and Cortisone—Their Promise and Limitations; Use and Abuse of Hormones in Obstetrics and Gynecology; Advances in Cardiology; Contributions to the Cancer Problem; Therapy of Peripheral Vascular Disorders; Therapy of Blood Diseases; Diagnosis of the Psychiatric Patient in General Practice, and Early Recognition and Treatment of Emergencies in the Newborn.

**Personals.**—Dr. Kentaro Shimizu, a professor of surgery at the Tokyo Imperial University Faculty of Medicine, is spending several months in Chicago at the Illinois Neuropsychiatric Institute.——At the annual meeting of the Board of Directors of the Hektoen Institute for Medical Research, December 5, Dr. Morris T. Friedell, research associate, was appointed chief of the radioactive isotopes laboratory and Dr. Irving F. Stein Jr. was appointed research associate of the institute.——Dr. Leon O. Jacobson, associate dean of the Division of Biological Science and assistant professor of medicine at the University of Chicago, has been appointed special consultant to the United States Public Health Service as a member of the hematology study section of the National Institutes of Health. Dr. Jacobson plans to attend the Sixth International Congress of Radiology in London next July and the meetings of the International Society of Hematology in Cambridge, England, in August. He will present a paper on "The Therapeutic Use of Radioactive Isotopes."——William H. Taliaferro, Ph.D., chairman and professor of bacteriology and parasitology, was recently awarded the Mary Kingsley Medal by the Incorporated Liverpool School of Tropical Medicine. The medal was bestowed in recognition of his contributions to tropical medicine.——Dr. Max A. Weisskopf, who recently retired as chairman of the department of obstetrics at St. Anthony de Padua Hospital, was presented a plaque commemorating 50 years of service.

## KENTUCKY

**State Society Service Awards.**—The Kentucky State Medical Association has presented its Distinguished Service Award to Dr. John Walker Moore, who served as dean of the Louisville School of Medicine for 20 years. He resigned as dean in July. The E. M. Howard medal, awarded annually for meritorious professional and public service, was presented to Dr. Addie M. Lyon, Frankfort, commissioner of welfare of the Commonwealth of Kentucky. He served as a county health officer for 16 years and as a county judge for four years and was superintendent of the Kentucky Training Home in Frankfort for 10 years. Dr. Lyon was appointed director of the Division of Hospitals and mental hygiene in 1941 and in 1948 assumed his present position. He also has been acting superintendent of Central State Hospital in Lakeland since 1945.

## LOUISIANA

**Appointments in Neurology and Psychiatry.**—Kathleen Young, psychologist for the Rockland State Hospital, Orangeburg, N. Y., and Dr. Henry E. King, senior research scientist, New York State Brain Research Project, have been appointed to the faculty of the department of psychiatry and neurology at Tulane University of Louisiana School of Medicine, New Orleans. Dr. Young will serve as assistant professor of clinical psychiatry in the school of medicine and assistant professor of psychology in the Tulane graduate school. Dr. King will serve as assistant professor of psychiatry and research psychology in the school of medicine.

## MICHIGAN

**Commissioners Health Conference.**—State Health Commissioner Albert E. Heustis has called a three day conference of health officers of Michigan's 54 local health departments, which serve 93 per cent of the state's population, in Lansing February 8-10 to consider public health programs carried on by local health departments with the assistance of the Michigan Department of Health. The conference, the first of its type in the state, is expected to result in recommendations not only for what the programs should include but how they should be developed. For the purposes of the conference, health officers of the state have been divided into five committees, each of which is to study, conduct discussions and develop recommendations in specific fields: infectious diseases, environmental and industrial health, fiscal policies and financing, interagency policies between state and local health departments and personnel, and other health services, including maternal and child health. The conference will be held in the state health department offices, Old DeWitt Road, Lansing.

## NEBRASKA

**Dr. Ryder Named State Health Director.**—Dr. Frank D. Ryder, Grand Island, assumed duties as director of the State Health Department November 15, succeeding Dr. Wallace S. Petty, Lincoln, resigned. Dr. Ryder is a native of Grand Island and began practice there in 1919 after graduation from Creighton University School of Medicine, Omaha.

## NEW JERSEY

**Schering Research Appointments.**—Drs. W. Alan Wright and Norman L. Heminway have been appointed to newly created positions of associate directors of clinical research of the Schering Corporation, Bloomfield, N. J. Dr. Wright received his M.D. degree from Temple University School of Medicine, in 1939. After private practice and serving as a medical officer with the Federal Trade Commission, he joined Schering's Division of Clinical Research in 1946. Dr. Heminway received his M.D. degree from the University of Pennsylvania School of Medicine, Philadelphia, in 1935. After several years in private practice he entered the army in 1941 and attained the rank of colonel. He is administrative assistant to Dr. Edward E. Henderson, director of clinical research, as well as associate director of clinical research.

**State Society to Aid in Safety Program.**—The Medical Society of the State of New Jersey is cooperating with the commissioner of motor vehicles to help determine whether the physical condition of drivers of automobiles is a significant factor in driver deaths. The program is twofold. Members of the society have been asked to perform on request examinations on automobile drivers over age 65 who have been involved in an automobile accident. Examinations, at a uniform fee of $5, do not include laboratory work or eye tests. The society is endeavoring to communicate with the family physician of the driver of every automobile involved in a fatal accident to determine whether the physician was aware of any physical abnormalities in the driver. The information is to reach the commissioner of motor vehicles only as an anonymous statistical item, and it will not be used in any legal process concerning the accident.

## NEW YORK

**Fellowships in Public Health Available.**—The New York State Department of Health announces fellowships in public health for physicians interested in entering this specialty as a career. Training in general public health consists of six or more months of supervised field experience in a selected district or county health department, followed by an academic year at one of the approved schools of public health. Training to qualify for a tuberculosis position consists of three months in a tuberculosis hospital, nine months' supervised experience in tuberculosis clinics and two months in general public health training in a selected district or county health department. Provision is also made for an academic year at one of the approved schools of public health for a selected physician in this type of training. Public health training is also given to physicians interested in one of the clinical specialties who desire to serve as specialists in maternal and child health, venereal disease or cancer control. This training consists of not more than two years and includes an academic year at an approved school of public health.

Information and application forms may be obtained from Dr. Franklyn B. Amos, director, Office of Professional Training, New York State Department of Health, Albany 1, N. Y.

### New York City

**Group Conducts Art Show.**—Physicians, surgeons, nurses and other members of the Beth Israel Hospital were exhibiters at the hospital's first annual art show December 13. Of the 37 represented, 35 found their inspiration outside hospital life in still life, landscapes, portraits and decorative themes. These include a portrait sculpture of the late Dr. Harvey Cushing by Dr. Leo M. Davidoff, a protégé of the brain specialist, and a portrait in pen and ink of Dr. John H. Garlock by Dr. Helmuth M. Nathan that won a second prize in an American Academy of Medicine show.

**Personals.**—Dr. Harold A. Abramson, assistant clinical professor of physiology, Columbia University College of Physicians and Surgeons, has been appointed chief of the allergy clinic at Mount Sinai Hospital.——Franklin Hollander, Ph.D., director of the gastroenterology research laboratory of the Mount Sinai Hospital, New York, delivered the December lecture before the Science Society of the Newark Colleges of Rutgers University, New Brunswick, on "The Problems of Gastrointestinal Ulcer."

**Two Million Volt X-Ray Machine in Cancer Hospital.**—A 2,000,000 volt x-ray machine will be installed some time next year in the new $8,000,000 Francis Delafield Hospital, which is located adjacent to the Columbia-Presbyterian Medical Center and is affiliated with the Columbia University College of Physicians and Surgeons. The new high voltage unit will permit the physician accurately to concentrate many times the intensity of radiation hitherto possible on the exact location of a deep-seated cancer. Francis Delafield Hospital is one of two new cancer hospitals nearing completion in Manhattan as a part of the current $42,000,000 municipal hospital construction program.

**Social Science in Medical Education.**—Experimental studies to attempt to determine what the social sciences may contribute to broadening medical and nursing education will begin in February at Cornell University Medical College and the Cornell University-New York Hospital School of Nursing, in cooperation with the Russell Sage Foundation. This work is expected to continue for about two years. Leo W. Simmons, Ph.D., now associate professor in the department of sociology, Yale University, New Haven, Conn., has been granted a leave of absence to direct the project. He will work in the Medical College within the department of medicine. His studies will be concentrated in the Psychosomatic Clinic of the New York Hospital. In the School of Nursing he will explore with the faculty the teaching areas for the preparation of nurses equipped to plan for the community health programs. Within this pattern, attention will be given to the health implications of family situations, problems of unemployment and old age, need for adequate housing, education and recreational facilities.

## NORTH CAROLINA

**Dr. Perlzweig Dies.**—William A. Perlzweig, Ph.D., professor of biochemistry and chairman of the department at Duke University School of Medicine, Durham, died in Duke Hospital December 10, aged 58. Dr. Perlzweig was best known for his discoveries in the field of nutrition.

**Annual Symposium.**—The seventh annual Watts Hospital Medical and Surgical Symposium will be conducted in the Watts Hospital and the Carolina Theater in Durham February 15-16. Participating in the program are: Drs. M. Edward Davis, Chicago; T. Hale Ham, Donald S. King, Robert R. Linton, Richard N. Overholt, Merrill C. Sosman and Shields Warren, all of Boston; Russell L. Haden, Crozet, Va.; Byrd S. Leavell, Charlottesville, Va.; R. Wayne Rundles, Durham; J. Mims Gage and William Parson, New Orleans, and Malcolm B. Dockerty, Rochester, Minn.

## PENNSYLVANIA

**State Society Honors Centenarians.**—For the third year all residents of the state who celebrate their one hundredth birthday will be honored for their longevity by the Medical Society of the State of Pennsylvania with the presentation of testimonial plaques. During 1949 fifteen centenarians were so honored; officers of the county medical societies made the presentations. In many instances the family doctor of the centenarian attended the ceremonies. The names and dates of birth of all those residents of Pennsylvania who will attain their one hundredth birthday during 1950 are requested and should be sent to the Medical Society of the State of Pennsylvania, 230 State Street, Harrisburg, so that plaques may be prepared and plans for presentation made.

### Pittsburgh

**Personal.**—Dr. Jonas E. Salk has been promoted to the position of research professor of bacteriology in the University of Pittsburgh School of Medicine. Dr. Salk is directing the work of the Medical School's Virus Research Laboratory concerned with problems in influenza and poliomyelitis.

**Bedford Lecture in January.**—Dr. Perrin H. Long, Baltimore, will give the annual Nathaniel Bedford Lecture before the Allegheny County Medical Society in Pittsburgh January 17. His subject will be "Recent Advances in Antibiotic Therapy and Their Effect on General Practice." Dr. Long is professor of preventive medicine in the Johns Hopkins Hospital, Baltimore. He is also consultant to the Veterans Administration, and the Secretary of Defense.

## WASHINGTON

**Rheumatic Fever Symposium.**—The Washington State Heart Association will hold its first annual scientific session January 13-14 at the Washington University School of Medicine auditorium, Seattle. The program will be devoted to various aspects of rheumatic fever. Among the speakers will be Drs. Benedict F. Massell, Boston; Charles H. Rammelkamp, Jr., Cleveland, and John J. Sampson, San Francisco. There will be no registration fee, and all members of the medical profession are invited to attend.

## PUERTO RICO

**Hospital Construction Approved.**—Construction plans and specifications for the hospital buildings to be constructed by the Puerto Rico government at the City of Ponce during 1950, at an estimated cost of $6,258,600, have been approved by the Insular Health and Interior departments. This first part of the project consists of a 400 bed hospital, physicians' residences, school for 200 student nurses, swimming pool and gymnasium, houses for personnel, service units, shops, laundry, machinery house, warehouses and a cafeteria. The project will be carried out in three stages: the first one, which will start in 1950, costing $6,258,600; the second, a 500 bed tuberculosis hospital costing $3,382,800, and the third a 1,000 bed mental hospital costing $6,644,500. This project forms part of the hospital facilities and public health program approved by the U. S. Surgeon General for Puerto Rico. Under this program a new tuberculosis sanatorium, costing over $4,000,000, is now under construction at Rio Piedras, in the vicinity of San Juan. This new hospital will provide 800 additional beds for tuberculosis patients in Puerto Rico.

## GENERAL

**Cerebral Palsy Meeting.**—The American Academy for Cerebral Palsy will hold its annual meeting at the Waldorf-Astoria in New York City Feb. 17-18. Scientific sessions will be open to visiting orthopedic workers and other physicians interested in cerebral palsy.

**Dr. Evans Receives Mickle Award.**—Dr. Herbert M. Evans, director of the University of California Institute of Experimental Biology, San Francisco, for his researches in endocrinology has received the Mickle Award of the Faculty of Medicine of the University of Toronto. The award is made once every ten years "to that individual who has contributed most significantly and in a practical way to the advance of medicine in any of its fields." Prof. Charles H. Best, chairman of the faculty committee, stated that Dr. Evans was chosen for "a long-continued series of studies relating to the isolation and final purification of five of the six anterior hypophyseal hormones."

**Parental Deaths and Divorces.**—Contrary to popular belief, disruption of family life in the United States is less frequent today than it was 60 years ago, according to the statisticians of the Metropolitan Life Insurance Company. This is because the drop in the number of families broken by the death of husband or wife has more than counterbalanced the upward trend of divorce. Since the early 1890's the divorce rate has climbed from about 3 per 1,000 married couples to 12 per 1,000 in 1948. During the same years the rate of marital dissolutions due to death of the husband or wife has fallen off from 30 to about 19 per 1,000. In 1890 less than 10 per cent of all broken families resulted from divorce; by 1946 divorce accounted for nearly as many as did death. With the readjustment to peacetime, however, the divorce rate receded and in 1948 was responsible for 38 per cent of all marital dissolutions.

**Society Elections.**—The American Chemical Society has chosen N. Howell Furman, Ph.D., Russell Wellman Moore professor of chemistry at Princeton University, as president-elect; Ernest H. Volwiler, Ph.D., North Chicago, Ill., took office as president January 1.——The American Association of Medical Colleges at its annual meeting in Colorado Springs chose Dr. Arthur C. Backmeyer, Chicago, president-elect and Dr. Franklin D. Murphy, Kansas City, vice president; Joseph C. Hinsey, Ph.D., New York, is president for 1950. Named to the executive council were Drs. Ward Darley, Denver, and Vernon W. Lippard, Richmond, Va.——The North Pacific Surgical Association at its recent meeting in Portland chose Dr. Siegfried F. Herrmann, Tacoma, as president and Dr. John A. Duncan, Seattle, secretary-treasurer.——At the meeting of the House of Delegates of the American Society of Anesthesiologists in New York December 9 the following officers were elected for the year 1950: Drs. Rolland J. Whitacre, East Cleveland, president; Urban H. Eversole, Boston, president-elect; J. Earl Remlinger Jr., Evanston, Ill., secretary, and Moses H. Krakow, Bronx, N. Y., treasurer.——Dr. Warren W. Furey, chief radiologist at Mercy Hospital-Loyola University Clinics and Children's Memorial Hospital in Chicago, has become president of the Radiological Society of North America, Inc. Officers named at the recent meeting were president-elect, Dr. John S. Bouslog of Denver and Dr. Donald S. Childs of Syracuse, N. Y., who was re-elected secretary-treasurer.

**Statement by Farm Bureau Federation.**—At its annual convention in Chicago December 15 the American Farm Bureau Federation adopted a statement on rural health which read, in part, as follows: State Farm Bureaus should give serious consideration to the desirability and possibility of offering scholarships whereby physicians, surgeons, dentists and nurses will be encouraged to establish themselves in rural areas. They should encourage local communities to cooperate in financing offices and equipment on an amortization basis necessary to attract doctors to locate in communities not now served by doctors. We believe the problem of improved health can best be met by the voluntary organization of state and county health councils which will encourage people to take advantage of the services available for any medical or dental care which they may require. We will continue to cooperate with other groups in providing better voluntary medical care for rural people. We will continue to support programs to deal with cancer, tuberculosis, venereal disease, poliomyelitis, crippled children, heart disease and rheumatic fever. We also endorse the American Red Cross Blood Bank Program. We favor voluntary plans providing medical, health, dental and hospital insurance. We urge that facilities of medical schools be expanded and that every effort be made to train more physicians, surgeons, dentists, nurses, technicians, general practitioners and public health doctors. We urge the full cooperation of rural populations with our established health units and existing health programs. We favor putting greater emphasis on preventive medicine. In states where permissive legislation for the creation of public health units does not exist, state farm bureaus should secure the enactment of such legislation. We favor reasonable appropriations for grants-in-aid to states for maternal and child health programs and also to assist states in the expansion of needed public health services and facilities. Federal grants should be made to states only on the basis of need, with state governments responsible for the allocation and administration of such funds. In the administration of the Hill-Burton Hospital Construction Act rural populations must have adequate representation on national and state advisory councils to insure practical application of the program at the local level. We are opposed to any form of national compulsory health insurance.

## CANADA

**Dr. Agnew Leaves Canadian Hospital Council.**—Dr. G. Harvey Agnew, executive secretary of the Canadian Hospital Council since its inception in 1931 and editor of *The Canadian Hospital,* has resigned to join a hospital consulting firm in New York. Dr. Agnew will direct offices in Toronto and will continue as head of the course in hospital administration at the University of Toronto. He will continue on a part time basis with the Canadian Hospital Council until next June.

**Child Health Section Formed.**—A newly formed division of the Health League of Canada will undertake popular education in maternal and child health and welfare. Heading the new division's voluntary directing committee are Drs. L. Nelles Silverthorne and Herman B. Van Wyck, both of Toronto. Surveys in the field of child and maternal health and an educational campaign in the interests of children will be undertaken. The gathering of statistics in the field will include information as to sickness and mortality rates and also studies as to the services available to prevent and cure disease in various parts of the nation. The new division will work in close cooperation with the Division of Child and Maternal Welfare of the Department of National Health and Welfare at Ottawa. Its directing committee is made up of nearly 50 prominent pediatricians, obstetricians, gynecologists and official representatives from each province.

# Marriages

HERBERT EDWARD LANE Jr., Brooklyn, to Miss Marie Antoinette Polcari of Portsmouth, Va., November 19.

JOSEPH HOWARD EARLY Jr., Hillsville, Va., to Miss Charlotte Taylor Ridge of Langhorne, Pa., November 12.

JAMES MARSHALL WILLETT, Jackson, Tenn., to Miss Jennie Lind Prater of Louisville, Ky., November 11.

WOODBERRY PERKINS, Greenwich, Conn., to Miss Mary Elizabeth Brown of New York, November 17.

PAUL WEBSTER BOWDEN to Mrs. Frances McAllister Simes, both of Richmond, Va., November 5.

NORMAN RIGHTHAND, Schenectady, N. Y., to Miss Josephine De Cecio of Brooklyn, recently.

ROBERT E. VOTTELER, Peoria, Ill., to Miss Helen Jean Cheney of Evanston, Ill., October 30.

THOMAS LEROY LAKE to Miss Judean Young, both of Berkeley, Calif., recently.

# Deaths

**William Creighton Woodward** ✠ first director of the Bureau of Legal Medicine and Legislation of the American Medical Association, died at his home in Washington, D. C., December 22, aged 82, of arteriosclerotic heart disease and congestive heart failure. Dr. Woodward was born in Washington Dec. 11, 1867, and in 1889 received his M.D. degree from Georgetown University School of Medicine in that city; in 1900 he received the Master of Laws degree and in 1925 the Doctor of Laws. He was appointed resident physician to the Central Dispensary and Emergency Hospital in 1892 and later physician to the poor and coroner of the District of Columbia. In 1901 he was admitted to practice law before the District of Columbia Court of Appeals, in 1917 the U. S. Supreme Court, in 1919 the Supreme Judicial Court of Massachusetts and in 1924 the Illinois Supreme Court. Dr. Woodward was professor of state medicine at his alma mater in 1894 and from 1893 to 1936 professor of medical jurisprudence. He was professor of medical jurisprudence also at George Washington University School of Medicine from 1900 to 1918, Georgetown University school of law from 1902 to 1935, Howard University College of Medicine from 1916 to 1918, Loyola University school of law in Chicago from 1925 to 1931 and University of Chicago Graduate School of Medicine and Rush Medical College from 1930 to 1939. From 1894 to 1918 he was health officer of the District of Columbia and from 1918 to 1922 health commissioner of the city of Boston. He had been president of the American Public Health Association, of the Conference of State and Provincial Boards of Health of North America and of the American Association for the Study and Prevention of Infant Mortality. Dr. Woodward was a member of the American Bar Association and an honorary member of the American Veterans Medical Association, International Association of Milk Inspectors and Conference on State and Provincial Health Authorities of North America. At one time he was secretary of the board of medical supervisors of the District of Columbia. During World War I he was a member of the general medical board of the Council on National Defense. He was chairman of the Section on State Medicine of the American Medical Association from 1899 to 1900 and in 1910 was appointed a member of the Council on Health and Public Instruction and placed in charge of its Bureau of Medical Legislation. He became director of the newly created Bureau of Legal Medicine and Legislation at the headquarters office in Chicago in June 1922 and served for eighteen years, retiring on Jan. 1, 1940 at his own request. He drafted the Federal Caustic Poison Act and a model state caustic poison law. Painstaking in his work and searching in his inquiries, Dr. Woodward faithfully served medicine. His basic contributions will continue to be of help to those who participate in medical affairs.

WILLIAM CREIGHTON WOODWARD, M.D.

**Samuel Carruth Haven** ✠ Morristown, N. J.; born in Morristown in 1875; Columbia University College of Physicians and Surgeons, New York, 1901; past president of the Morris County Medical Society; past president of the city board of health; on the Morris County medical advisory board in World Wars I and II; served many years as president of the medical board at the Morristown Memorial Hospital, where he was attending physician and was instrumental in starting the pediatric ward and laboratory; attending physician at All Souls' Hospital and Shonghum Mountain Sanatorium; member of the McKean Medical Historical Society; on the advisory board of the Visiting Nurses' Association; died November 21, aged 74, of emphysema, chronic bronchitis and asthma.

✠ Indicates Fellow of the American Medical Association.

**Ulrich Adolf Friedemann,** Great Neck, N. Y.; born in Berlin, Germany, May 7, 1877; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1900; for many years affiliated with Jewish Hospital in Brooklyn, where he was consultant on the staff of Kings County Hospital; formerly served on the faculty of the University of Berlin, with the Robert Koch Institute and Rudolf Virchow Hospital in Berlin; formerly member of the National Institute for Medical Research in London and Dunham lecturer at Harvard University, Boston; member of the New York Academy of Sciences, American Association of Immunology and the American Association for the Advancement of Science; died November 15, aged 72.

**Walter Johnston Cree,** Detroit; born in Detroit, 1861; Michigan College of Medicine, Detroit, 1883; at one time on the faculty of Michigan College of Medicine and Surgery; member of the American Medical Association; reserve officer of the U. S. Public Health Service; served as secretary of the Detroit Medical Library Association, secretary and historian of the Wayne County Medical Society, secretary of the Detroit Obstetrical and Gynecological Society and treasurer and historian of the Detroit Academy of Medicine; for many years medical examiner for the Metropolitan Life Insurance Company; in 1936 received the honorary degree of master of science from Wayne University; died November 9, aged 88, of chronic myocarditis.

**Orin Author Ogilvie** ✠ Salt Lake City; born in Richfield, Utah, May 29, 1895; University of Pennsylvania School of Medicine, Philadelphia, 1927; for many years on the faculty of the University of Utah School of Medicine; specialist certified by the American Board of Pathology; member of the College of American Pathologists and American Society of Clinical Pathologists; immediate past president of the Utah State Medical Association and past president of the Salt Lake County Medical Society; for many years pathologist at Salt Lake General, Holy Cross, and St. Mark's hospitals; founder and director of the Wasatch Laboratories; died November 8, aged 54.

**George James Joseph Lawrence,** Flushing, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1907; member of the American Medical Association; a retired major general of the New York National Guard; state commander of the American Legion, 1932-1933; served on the Mexican border and in France during World War I; past president of the Queensboro Surgical Society; affiliated with the Flushing Hospital and Dispensary; vice president of the Flushing Savings Bank; died November 9, aged 68, of carcinoma of the prostate.

**Max Jacobs Abramson** ✠ Los Angeles; College of Physicians and Surgeons, Medical Department of the University of Southern California, Los Angeles, 1911; specialist certified by the American Board of Obstetrics and Gynecology; on the staff of Cedars of Lebanon Hospital; died November 12, aged 68, of chronic myelogenous leukemia.

**Samuel Milligan Anderson,** Wichita, Kan.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; member of the American Medical Association; served on the staffs of St. Joseph's and Wichita hospitals; died in California Hospital, Los Angeles, November 11, aged 73.

**George Elliott Atwood Jr.,** Waycross, Ga.; University of Georgia Medical Department, Augusta, 1900; member of the American Medical Association; for many years city and county health officer; served in the medical corps of the U. S. Army during World War I and until 1925; spent three years in Puerto Rico, where he was post surgeon at San Juan with the 65th Infantry Division; died recently, aged 72, of heart disease.

**Ernest H. Ball,** Charleston, W. Va.; Maryland Medical College, Baltimore, 1909; died November 27, aged 61, of heart disease.

**Thomas Jefferson Beattie,** Kansas City, Mo.; Kansas City Medical College, 1885; University of the City of New York Medical Department, 1886; affiliated with St. Joseph Hospital; member of the American Medical Association; died November 23, aged 86, of chronic myocarditis and arteriosclerosis.

**Stanley Brady** ✦ New York; Columbia University College of Physicians and Surgeons, New York, 1905; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; past president of the medical board and for many years director of the division of pediatrics at St. Vincent's Hospital; on the staff of French Hospital; died November 23, aged 68.

**John J. Buscaglia** ✦ Buffalo: University of Buffalo School of Medicine, 1925; served in the medical corps, Army of the United States, during World War II; affiliated with Columbus Hospital; died November 13, aged 48, of coronary thrombosis.

**Edwin Frank Chamberlain,** San Diego, Calif.; Northwestern University Medical School, Chicago, 1910; member of the American Urological Association; died November 16, aged 62, of cerebral hemorrhage.

**Ole Anthony Christensen,** Hawkins, Wis.; Chicago Medical College, 1891; died in St. Mary's Hospital, Ladysmith, recently, aged 85, of carcinoma.

**Charles Clark,** San Francisco; Bennett Medical College, Chicago, 1893; formerly member of the state board of medical examiners; died in St. John's Hospital November 7, aged 80.

**John Joseph Corrigan,** Hazleton, Pa.; Jefferson Medical College of Philadelphia, 1896; member of the American Medical Association; died November 12, aged 79.

**Dudley V. Courtright** ✦ Circleville, Ohio; Starling Medical College, Columbus, 1897; past president of the Pickaway County Medical Association; died in Paris, Ky., November 2, aged 74, of injuries received in an automobile accident.

**Tello Jaen d'Apery** ✦ Philadelphia; Jefferson Medical College of Philadelphia, 1905; died November 19, aged 73.

**Joseph de Silva** ✦ Rock Island, Ill.; Northwestern University Medical School, Chicago, 1893; formerly served as a member of the public library board, city physician and as medical examiner for the draft board during World War II; one of the founders and affiliated with the Rock Island County Tuberculosis Sanatorium; a trustee of the penitentiary in Joliet and the Lincoln (Ill.) State School and Colony; died in St. Anthony's Hospital November 10, aged 80.

**William Brown Ford** ✦ Milwaukee; Rush Medical College, Chicago, 1903; formerly on the faculty of the Marquette University School of Medicine; member of the American Trudeau Society; part time assistant superintendent of the tuberculosis division of the city health department for many years; on the staffs of St. Joseph, Deaconess and Milwaukee hospitals; died December 1, aged 75, of carcinoma of the stomach.

**John Walter Goodsell,** Sandy Lake, Pa.; Pulte Medical College, Homeopathic, Cincinnati, 1898; served during World War I; died in Deshon Veterans Hospital, Butler, November 18, aged 76, of cerebral and cardiac arteriosclerosis.

**Ira B. Gordon** ✦ Cleveland; Pulte Medical College, Homeopathic, Cincinnati, 1891; died in the Lakewood (Ohio) Hospital October 26, aged 78, of acute myocardial infarction.

**Wilfred George Grandison** ✦ Boston; Tufts College Medical School, Boston, 1901; an Associate Fellow of the American Medical Association; affiliated with Carney and St. Elizabeth's hospitals; died November 6, aged 73, of asthma, emphysema and bronchopneumonia.

**Samuel D. Greenwood,** Neenah, Wis.; Chicago Homeopathic Medical College, 1900; the Hahnemann Medical College and Hospital, Chicago, 1905; served on the staff of Theda Clark Memorial Hospital; died recently, aged 80, of carcinoma of the lung and of the prostate.

**Arthur Field Harrington** ✦ Muskegon, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1903; fellow of the American College of Surgeons; affiliated with the Hackley and Mercy hospitals; died November 7, aged 73, of arteriosclerosis.

**Addison M. Harrison** ✦ Kansas City, Mo.; Beaumont Hospital Medical College, St. Louis, 1892; died November 26, aged 80, of coronary thrombosis, hypertension and diabetes mellitus.

**Alfred Taylor Hawes,** Lynn, Mass.; University of Vermont College of Medicine, Burlington, 1900; member of the American Medical Association; an honorary member of the staff of Lynn Hospital; found dead December 2, aged 75, of heart disease.

**Charles Lawson Housel,** Denver; Lincoln (Neb.) Medical College of Cotner University, 1907; Illinois Medical College, Chicago, 1908; member of the American Medical Association; died in Fitzsimmons General Hospital November 4, aged 71.

**Hannah Luella Hukill,** Glendale, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1899; formerly on the faculty of Rush Medical College in Chicago; died November 2, aged 78, of heart disease.

**Thomas Herbert Infield,** Zanesville, Ohio; Baltimore Medical College, 1897; affiliated with the Bethesda Hospital; died in a hospital at Columbus November 4, aged 79, of bronchopneumonia.

**Frederick George Linde,** San Francisco; University of California Medical School, San Francisco, 1916; formerly on the faculty of his alma mater; specialist certified by the American Board of Orthopaedic Surgery; member of the American Academy of Orthopaedic Surgeons and the American Medical Association; affiliated with the San Francisco Hospital and the Franklin Hospital, where he died November 7, aged 59, of coronary occlusion.

**William Barnes Litten** ✦ West Bedford, Ohio; Columbus Medical College, 1880; served as a member of the Coshocton County Medical Board; examiner for Union Central, New York Central and Farmers and Traders Insurance companies; director of First National Bank; died November 23, aged 93, of arteriosclerotic heart disease.

**Robert Henry Lott** ✦ Carroll, Iowa; State University of Iowa College of Medicine, Iowa City, 1913; died recently, aged 66, of uremia.

**Cornelia Adeline McConville,** Brooklyn; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1894; died November 19, aged 80.

**Frederic Leslie McCrea** ✦ Port Jefferson, N. Y.; Long Island College Hospital, Brooklyn, 1907; chief of the obstetric department and past president of the medical board, Mather Memorial Hospital; died November 11, aged 68.

**Milton Berlin McDowell,** Chadron, Neb.; Omaha Medical College, 1902; served as health officer; on the staff of Chadron Municipal Hospital; died in Lincoln November 11, aged 74, of acute coronary thrombosis.

**Seth A. Mereness,** Oneonta, N. Y.; Albany (N. Y.) Medical College, 1890; died in the Mary Imogene Bassett Hospital, Cooperstown, October 29, aged 82, of adenocarcinoma of the rectum and benign hypertrophy of the prostate.

**Samuel Edwin Milliken,** Dallas, Texas; University of Louisville (Ky.) Medical Department, 1887; member of the American Medical Association; fellow of the American College of Surgeons; died recently, aged 83, of rupture of dissecting aortic aneurysm and arteriosclerosis.

**Martin Alvin Mortensen,** Santa Monica, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1899; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the American Heart Association; served on the staff of the Battle Creek (Mich.) Sanitarium; died November 8, aged 77.

**James Murray,** Conley, Ga.; Birmingham Medical College, 1915; died November 3, aged 69.

**James Timothy O'Hora** ✦ Detroit; Rush Medical College, Chicago, 1926; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; served in France during World War I; affiliated with the Woman's Hospital and Children's Hospital; died November 9, aged 54, of coronary occlusion.

**James Oscar Sanders,** Anderson, S. C.; Maryland Medical College, Baltimore, 1900; member of the American Medical Association; died September 22, aged 74, of heart disease.

**James A. Sewell,** Atlanta, Ga.; Southern Medical College, Atlanta, 1893; died September 11, aged 80, of intestinal obstruction.

**Warren L. Story,** Ashburn, Ga.; Atlanta Medical College, 1888; member of the American Medical Association; died in Tifton (Ga.) Hospital September 24, aged 84, of heart disease.

**John George Wagner** ✦ River Bank, N. J.; Jefferson Medical College of Philadelphia, 1913; also a graduate in pharmacy; specialist certified by the American Board of Radiology; member of the American College of Radiology; affiliated with the Zurbrugg Memorial Hospital, Riverside; died September 22, aged 64.

**David Scyrus Warner,** Center Moriches, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1888; died November 13, aged 85.

# Foreign Letters

## PARIS

*(From Our Regular Correspondent)*

Nov. 7, 1949.

### The Surgeon's Responsibility

The surgeon's responsibility toward the patient is differently interpreted by various courts. In principle, the patient's consent has to be obtained prior to surgical intervention, this obligation proceeding from the respect of human liberty, but the problem remains of determining how far the surgeon has the right to extend his intervention in the course of an operation. Three cases have appeared recently in courts. The first case was that of a person who had had a tumor in the left arm for years. After having diagnosed a small benign tumor, the surgeon recommended an operation which he thought to be simple and without functional sequela; the patient agreed. In the course of the operation, the surgeon found a tumor difficult to isolate, inserted on the radial nerve and appearing to him as malignant. He extirpated it without advising the patient of the possible consequences and without asking for his consent. Since he had been unable to anticipate this, he postponed a nerve graft to a later date. In spite of the graft, performed five months later, and electrotherapy, radial paralysis set in, interfering with the use of the left arm. The patient demanded compensation, and the court condemned the surgeon, not on account of the error of diagnosis but on account of the lack of the patient's consent, stating that the surgeon ought to have interrupted the operation, unless there was a necessity or an urgency endangering the patient's life. In another case, a patient had given consent to an operation but had specified that she would not submit to any operation which would prevent pregnancy. In the course of the operation, the surgeon found that, instead of the hysteropexy that had been considered, an ovariotomy was necessary, and he performed it. The patient lodged a claim, but the court exonerated the surgeon, stating that the operation had been performed with the patient's consent, who had voluntarily submitted to an operation in the uterine area to be relieved of her pain. The third case concerned the limitation of responsibility of the surgeon as regards postoperative treatment. After a successful operation, the patient was returned to her room. Nurses had placed an electric arc in her bed for warmth, which caused a burn on the leg. This resulted in permanent disability in spite of long treatment. The patient sued the clinic for damages, but the latter charged the surgeon with responsibility. The court refused to admit the surgeon's responsibility, as the accident had occurred during postoperative care for which the hospital was responsible. This was the first time that a French court made a distinction between the postoperative treatment within the scope of surgery and attendance incumbent, usually, on the hospital.

### Surgical Intervention in Mitral Stenosis

This operation pertains to mitral stenosis of the Gallavardin type, clinically characterized by dyspnea, edema of the lung, hemoptysis, normal tension in the systemic circulation and hypertension in the pulmonary circulation. At a radiologic examination it is noted that the heart is small, the right ventricle is not dilated and there are shadows of pulmonary edema. D'Allaines and Lenègre and his co-workers have evolved an operation (intrathoracic, but extracardiac) for the deviation of the lesser circulation into the greater by short circuiting both circulations by anastomosis of the right superior vein into the azygos vein or into the superior vena cava. The best type is the terminolateral anastomosis. Surgical treatment was successful in 7 of 11 patients. Five experienced a spectacular result and have resumed normal activity; all functional disorders disappeared. Two patients were improved for two months only, probably on account of a secondary thrombosis of the anastomosis. Three patients, between 30 and 50 years of age, died; they had shown beginning right-sided asystole, which the authors now consider a contraindication to operation. In the last case anastomosis was impossible and a simple ligature of the pulmonary vein was effected. Their study was reported on Oct. 26, 1949, to the Academy of Surgery.

### Treatment of Diabetic Coma

In diabetic coma, one of the most important disorders of glycidic metabolism is related to pyruvic acid. Insulin does not appear to act in a constant manner on this alteration. R. Boulin, P. Uhry, F. V. Meyer and S. Bonfils presented a new method of treatment with cocarboxylase and riboflavin. Ten patients with diabetic coma were treated by intravenous injection of 60 units of insulin in two doses of 100 mg. cocarboxylase and 10 mg. riboflavin in the first hour. During the next two hours 15 units of insulin were injected every quarter of an hour; after the third hour dextrose in isotonic sodium chloride solution was also injected. The treatment was continued until the alkaline reserve reached 50 volumes. Results were excellent. Normalization of the alkaline reserve resulted within an average of six hours. The average dose of insulin used was 336 units, with only 120 units in 1 patient. A control series of 10 patients treated by the old method resulted in 2 deaths. Normalization of the alkaline reserve occurred in ten and a half hours; the quantity of insulin used was 2,958 units. At the meeting of June 24, 1949, the authors stressed that, subject to more extensive study, the new method appeared to represent progress.

## TURKEY

*(From Our Regular Correspondent)*

ANKARA, Nov. 20, 1949.

### Acute Glanders Responds to Streptomycin

Glanders is rare in Turkey. According to the statistics of the Ministry of Health and Social Assistance there have been only 18 cases of human glanders during the last ten years, all fatal. A memorial service is held annually in commemoration of the three veterinaries who died of laboratory infection with glanders twelve years ago.

Dr. Necati Selvi and Dr. Zafer Paykoç of the Ankara General Hospital infectious diseases department successfully treated a patient with acute glanders with streptomycin. On May 11, a farmer aged 37 was admitted to the hospital. Ten days previously, while working in the field, the patient was suddenly overcome with shivers, severe headache, pain in the upper and lower extremities, on which appeared dark red-blue painful swellings a few days later. Two weeks before the onset of the disease the patient's horse had died of an unidentified disease (there was no veterinary in the village). On admission the patient was semiconscious, had a temperature of 39.2 C. (102.8 F.), a weak pulse (rate 125) and a coated dry tongue and was in great pain. On his right arm he had seven soft abscesses about the size of walnuts, eight of the same kind and size in the hollow of the knee and on the upper part of the chest 27 smallpox-like pustules. Bloody pus from the abscess of the arm revealed gram-negative bacilli here and there. From a culture made the same day, Dr. Ali Korur, bacteriologist in charge, recovered gram-negative bacilli, Malleomyces (Pfeifferella) mallei. The next day, May 12, the patient's leukocyte count was 20,300, stab forms 13, segmented cells 71 and lymphocytes 16; eosinophils and monocytes were absent. Examination of the patient's other organs did not reveal anything special. The diagnosis of acute glanders being confirmed, the patient was given an injection of 2 Gm. of streptomycin, 600,000 units of penicillin and 6 Gm. of sulfadiazine by mouth for ten days. On May 16, small nodules and pustules, one of which grew and suppurated, developed on the face and forehead. The next day typical glanders bacilli were

recovered from the mucous membrane of the nose. On May 18, the temperature had decreased to between 37 and 38 C. (98.6 and 100.4 F.), the abscesses on the arms and legs began to diminish in size, some spontaneously opened, releasing pus, and the patient's condition suddenly improved. The temperature became normal on May 22, and with the exception of one under the right arm the abscess drained spontaneously and closed. Thereupon treatment with penicillin and sulfadiazine was discontinued, and the patient was given only a daily dose of 1 Gm. of streptomycin. On May 23 Dr. Sadik Gören, veterinary microbiologist, made serologic tests from blood and pus of an abscess. The result of the agglutination test was slightly positive (1:100), and the deviation of the complement was strongly positive. In a fresh pus preparation glanders bacilli were absent, but potato mediums revealed the characteristic Malleomyces mallei. No reaction was produced by 0.5 cc. of the pus inoculated into the peritoneal cavity of a male guinea pig. Another male guinea pig inoculated in the same way with a culture from potato mediums had orchitis three days afterward, and on the sixth day an abscess developed. Necropsy revealed a putrified sacrocele, and from its pus the characteristic glanders bacilli were produced on special mediums (Strauss reaction). The result of the agglutination test of the antigen produced from the pus culture was negative and the deviation of the complement strongly positive. On May 25, the patient had completely recovered and, on his request, was discharged. He was visited at his village three times, July 31, August 8 and August 21; in three months there had been no relapse and he was in good health. During treatment the patient received 2 Gm. of streptomycin daily, and within ten days the temperature became normal; thereafter, until his discharge, the patient was given only 7 Gm. Penicillin and sulfadiazine were used as adjuncts; there were no toxic effects.

This is probably the first case of acute glanders in a human being successfully treated with streptomycin with supplementary treatment with penicillin and sulfadiazine as a precautionary measure. The result of treatment with streptomycin on the experimentally induced glanders in animals is being investigated, and results will be published separately.

### International Congress of Comparative Pathology

The first two international congresses of comparative pathology were held in Paris in 1912 and 1931, the third was held in Athens in 1936, the fourth in 1939 in Rome, where it was decided that the fifth congress would be held in Istanbul in 1942. It was held there at the Shale Kiosk of the Yildiz Palace, the residence of the late Sultan Abdul Hamid II, from May 13 to 20, 1949, under the presidency of Prof. Nihad Reshad Belger of Istanbul University Medical School. Professor Belger's opening address was followed by an address of welcome by the Prime Minister, Prof. Shemseddin Günaltay, and Dr. Kemali Bayizit, the Minister of Health and Social Assistance. There were 42 communications concerning matters of medicine, veterinary and plant biology from Turkey, fifteen from Italy, fourteen from Great Britain, thirteen from France, six from the United States, five from Greece, four from Spain, three from Belgium and one from Iraq. There were also delegates from Canada, Holland and Hungary.

Prof. G. Ramon of the Paris Institute of Pasteur reported on the principles of anatoxin and antivirus. Prof. Kenneth M. Smith of Cambridge presented a communication on a new plant virus. Prof. P. Rondoni of Italy reported on hydrocarbons in relation to cancer and Prof. Zavagli of Italy on microbic interactions in prophylaxis of infectious diseases. Professor Oberling of France presented an interesting report concerning the neoplastic process and the ultravirus, and, on the basis of his many animal experiments, expressed a belief in viral-microbic causation of cancer. Prof. Ph. Schwartz of Istanbul University Medica School defended the cell etiology of cancer. Sir Howard Florey, co-discoverer of penicillin, reported on tissue reaction against micrococsin, with a comprehensive review of this newly discovered antibiotic. Prof. E. H. Lennette, W. H. Clark and H. B. Dean reported on Q fever in Northern California. Prof. M. Bariéty of the Paris Medical Faculty presented a paper on tuberculosis in relation to allergy and immunity and also a lecture on the treatment of tuberculosis at the Guraba Hospital, Topkapu, Istanbul, a university teaching unit.

Because of the number of reports, separate committees were set up on the fourth day. Some communications from Turkey were: Histoplasmosis in Turkey, by Ord.Prof. Tevfik Saglam; Mixed Intoxication in Miocardiae, by the late Prof. Akil Mouhtar Özden and Dr. Hatice Açikalin; Problem of Muscular Tone, by Prof. H. Winterstein; Hydatid Cysts in the Nervous System, by Ord.Prof. Fahreddin Kerim Gökay; Epidemiology of Q Fever, by Dr. S. Payzin; Distomum Hepaticum and Distomatosis in Turkey, by Sureyya Aygün, Doctor of Veterinary Medicine; Cancer Tumor Caused by Pseudomonas Tumeficient, by M. Karman and Mel. Karman; Local Streptomycin Treatment in Mucous Tuberculosis of the Uterus, by Prof. Tevfik Remzi Kazancigil; Kala-azar in Turkey, by Dr. N. Fakaçelli; Ornithodorus Lahorensis, by Dr. S. Oytun; Zoocysts in Turkey, by Dr. B. Alkan; Brucellosis in Turkey, by Said Bilal Golem, Doctor of Veterinary Medicine; and Intestinal Pneumatosis, by Dr. M. Yenerman.

Hospitals, clinics, mosques and museums were visited, excursions were made along the Bosporus, along the southern coast of the Black Sea to Rize, to the Prince's Islands in the Sea of Marmora, to Bursa and to the Yalova Springs, where a banquet was given by Dr. Kemali Bayizit, the Minister of Health. A special plane took members to Ankara, where the medical school, hospitals, clinics and historical places were visited.

The next congress is to be held in Ghent, Belgium, in 1954.

## OSLO

*(From Our Regular Correspondent)*

Dec. 6, 1949.

### The Norwegian Army Medical Service

Dr. Karl Evang, head of the Norwegian Public Health Service, addressed the annual meeting of the Norwegian Red Cross Society in the fall of 1949 on the workings of this service in the last war. During World War II the fighting services and civilians showed a genius for improvisation, which had virtue but at times became almost a vice. Indeed, it was overimprovisation which was responsible for the worst mistakes: Far too many doctors, nurses and other personnel were inspired to join combatant units and deserted their permanent jobs, in which they were irreplaceable. When and if war breaks out again in Norway, Dr. Evang expects local medical officers of health in most instances to remain where they are, attending to the medical requirements of areas with which they are already familiar. Dr. Evang reminded his listeners that even in total war, where there is intense participation by the community, only 10 per cent of the population is under arms and in civil defence units. Matters would be rather simple if the medical authorities could concentrate on these 10 per cent, "but total war makes it even more necessary to pay constant attention to the remaining 90 per cent of the population." The situation with regard to supplies of medical stores is worse today than it was in 1939, and government grants are apt to hang fire. There are at present some 28,000 hospital beds available, and this number must be doubled for wartime purposes. To staff the supplementary wartime beds, Dr. Evang needs 600 doctors, 6,000 nurses and other personnel, totaling 13,500. Early in 1950 the Norwegian Parliament will be called on to provide legislation necessary for the introduction of the various changes which Dr. Evang and his collaborators have studied. Money is still lacking; 900,000 kroner are needed merely to provide the necessary quantity of dry plasma.

### Inconsiderate Hospital Doctors and Frustrated Nurses

The Norwegian housewife knows that, unless she treats her domestic servant tactfully, she may lose this help at a moment's notice. Fortunately, the Norwegian nurse does not leave as readily. She has *esprit de corps,* the traditions of her profession and the welfare of her patients to safeguard, but it is possible she may have some grievances. The editors of the journal of the Norwegian Medical Association (*Tidsskrift for Den Norske Lægeforening*) evidently have recognized this and have published a candid letter on the subject by Elisabeth Ordrup, representing the Norwegian Nursing Association. She points out that, in conversation with various nurses, she has gained the impression that they find themselves unequal to their tasks because of the inconsiderate claims of doctors inclined to assume that a nurse has nothing else to do than to wait on them. For example, the timing of the doctors' rounds may be so erratic that the patients' dinners, which the nurses serve, are a half-hour or more late. Having stressed the state of "dangerous irritability" to which hospital nurses are reduced for want of due appreciation of their needs, Elisabeth Ordrup ends on a conciliatory note: "It may be assumed that the failings in cooperation between doctors and nurses in a hospital are not due to want of good will or understanding from either side but to an inadequate appreciation of each other's difficulties."

## MEXICO

*(From a Special Correspondent)*

Nov. 22, 1949.

### International Congress of Military Medicine and Pharmacology

The Twelfth International Congress of Military Medicine and Pharmacology met in Mexico Oct. 23-29, 1949, under the sponsorship of the president of the republic, Dr. Miguel Aleman. This was the first time that the convention was held in Latin America. The lectures at the opening sessions were presented by the president of the congress, Brig. Gen. Ignacio Landero Ramirez and by Generals Meuli and Voncken, who formerly were president and secretary, respectively, of the International Committee. They emphasized the wide range of information offered at these sessions to the military physicians, not only from the point of view of the technics of medical science but also as regards the rules which ought to govern the medical profession in time of war. In this connection it is essential to emphasize the important role which the International Committee of Military Medicine has played in the revision of the conventions of Geneva. Thanks to these efforts the principle of noncaptivity of medical personnel has been maintained, and it has also been possible to maintain on this basis the International Red Cross.

General Landero Ramirez emphasized the role of the military medical profession, which represents an ideal of peace and humanity even in wartime. He also emphasized the importance which ought to be attached to the creation of and to the instruction in an international medical code.

The sessions of the twelfth congress were completely successful, thanks to the vigilance of Col. G. Suarez Torres, who was the general secretary, and numerous works were presented and are herein summarized.

#### MEDICOSOCIAL PROBLEMS OF THE ARMY

Since the end of the war attention to social problems has been greatly extended in the armed forces, because of the national character of modern armies. Two phases dominate the training and instruction of the soldier: (1) giving him the highest possible potential for effective combat, and (2) preparing him for readaptation into the civilian life of the nation after demobilization. Efforts should be made to reconcile these two seemingly contradictory tendencies.

The Army thus must be a school for civilian life. This is the aim of the new science which some have tentatively called sociatry. It would be necessary to create adequate facilities for this purpose and every military physician should be instructed that he will be able to fill the role which these new tendencies in social medicine place on him.

#### MAXILLOFACIAL WOUNDS

The final results depend primarily on the first aid given persons with maxillofacial injuries. Care should be taken in the organization of the medical services of the army to create units composed of specialists in maxillofacial injuries. These units should include otorhinolaryngologists, oculists and neurosurgeons. Persons with lesions of the face should likewise be evacuated to be cared for in such units. Satisfactory results can be obtained only if the injured person is in the care of these units from the beginning. In the forward areas, only aid of extreme urgency can be given.

#### PSYCHOSES OF WAR

An extensive and well documented report of Dr. Paraire, professor at Val-de-Grace in Paris, served as a basis for these conclusions: If one studies the several communications which were presented, it becomes apparent that the psychiatric disorders were frequent during the last world war, but it can be affirmed that the role of the war itself has been overestimated in the causation of the psychoses. The psychoses are due particularly to individual predisposition. These have been aggravated and become manifest because of superimposed factors such as fatigue, difficulties of life during war, anxiety and separation from familiar surroundings.

Without doubt the treatment of psychiatric disturbances has made great progress, mostly because of psychoanalysis, but for the armies prevention is especially important. This can be accomplished by strict selection, which should eliminate from army service all those predisposed to psychiatric disturbances. To accomplish this the hope was expressed that all countries would combine their investigations to permit the development of formulas to discover those who are predisposed to mental disorders.

#### PATHOLOGY AND TREATMENT OF LESIONS CAUSED BY ATOMIC BOMBS

One of the questions of greatest interest was the study of the pathologic aspects and treatment of lesions caused by the atomic bomb. After the presentation of a film showing the pathologic material at Nagasaki and Hiroshima and after the extensive and well documented presentation by Gen. George Armstrong and Col. H. Glorieux, the congress unanimously recommended that for humanitarian reasons international laws prohibit the employment of atomic weapons.

Since the civilian population will be affected as much as the armies by atomic attacks, it is desirable that there be created in each country an organization comprising medical, civilian and military authorities to study and come to an agreement regarding measures to be taken in the defense against atomic weapons and that the medical personnel, civilian as well as military, be instructed in the prevention, pathology and treatment of atomic lesions. The hope was expressed that the medical authorities of various countries would arrange for periodic exchanges of medical information, technical instruction and discoveries in the sphere of atomic pathology.

#### MINIMAL RATION OF SOLDIERS IN COMBAT

Rations of soldiers in combat was the object of papers describing the care which military medicine and hygiene have given to this problem. The congress established that a normal ration for a soldier should take into account his activity and that its energy value should comprise 3,500 to 4,500 calories. It must contain: 70 to 140 Gm. protein, 60 to 150 Gm. fat, 600

to 750 Gm. carbohydrates, 5,000 units of vitamin A, 1.5 to 2.5 mg. vitamin $B_1$, 1.5 to 2.5 mg. riboflavin, 15 to 25 mg. nicotinic acid, 50 to 100 mg. vitamin C, 12 mg. iron, 0.8 to 1.5 Gm. calcium, 1.5 to 2 Gm. phosphorus and 8 to 15 Gm. salt. The minimal ration must meet physiologic needs, with an energy value not less than 3,000 calories; it should provide 70 to 130 Gm. protein, 30 to 70 Gm. fat, 300 to 500 Gm. carbohydrate and the aforementioned quantities of vitamins. Because of the emergencies and conditions of modern war, there should be an extraordinary minimal ration (pocket ration, famine ration). This should have a minimal energy value close to the basal metabolism: 1,500 to 1,800 calories, represented by: 30 to 40 Gm. protein, 40 to 60 Gm. fat, 250 to 350 Gm. carbohydrate and vitamins.

The combative efficiency of a military unit depends largely on the food that is furnished. The commander must see that special personnel is trained to prepare meals that are satisfying and strengthening. Conservation, packing and transportation of the food supply must be done according to suitable hygienic technics.

### AIR-BORNE MEDICAL SERVICE FOR COMBAT FORCES

Because of the development of large scale military operations, evacuation by air must become the method of choice for evacuating the wounded. Unfortunately, it will not be possible to employ aircraft flying under the protective sign of the Red Cross for transportation in the forward areas. For tactical and economic reasons, airplanes transporting war materials and combat personnel to the front will be used on their return flight to evacuate the wounded. Under these conditions it will be impossible to employ strictly medical aircraft facilities. To obtain satisfactory results it is essential that the air forces of the general staffs include medical men.

### CONSERVATION OF MEDICAL SUPPLIES DURING STORAGE

A technical study of the conservation of drugs and medical supplies and their packing for shipment was presented. All necessary measures should be taken to insure intact conservation by means of special packing and attention to minute details during preparation.

During and at the end of the congress numerous receptions were organized by the governmental authorities of Mexico, especially the minister of foreign affairs and the minister of public health.

At the closing session, personally presided over by the president of the republic, France extended an invitation, through the general medical inspector, L. Jame, to hold the Thirteenth International Congress of Military Medicine in Paris in 1951. The following subjects have been put on the calendar:

Principles of Tactical and Material Organization of First Aid in Case of Massive Inflow of Wounded as a Result of Major Attacks—reporting countries: India and France.

Instruction of Personnel of the Medical Corps (Active and Reserve); Planning of the Career of the Military Physician—reporting countries: Uruguay, Mexico and France.

Medical Problems Involved in Aerial and Submarine Navigation—reporting countries: United States and France.

Medical Aspects of Defense—reporting countries: Great Britain and France.

Present Role of Military Pharmacist in Times of War—reporting countries: Spain and France.

## Conference in Havana, Cuba

At the end of the Twelfth International Congress of Military Medicine and Pharmacy in Mexico, the Cuban government invited the members of the International Committee and all participants in the congress to attend a series of medicomilitary conferences in Havana, Cuba, Nov. 6-8, 1949.

The Medical Service of the Cuban army had intensified its efforts to arrange within three days a program which was adjudged a great success by all participants in the congress. The opening session was distinguished by a lecture given by Cesar Salaya, professor of international law of the Legal Faculty of Havana, who gave a historical survey of all efforts which the International Committee of Military Medicine had made in order to humanize war. He explained how, as the result of the collaboration of physicians and jurists, the Project of Monaco which is still the foundation of all international medical ethics, came into being in 1934.

### INSTRUCTION IN THE INTERNATIONAL MEDICAL CODE

General Voncken pointed out the necessity for a course of instruction in the international medical code, which comprises, in addition to the principles for governing all medical activities in times of war, instruction for all civilian and military physicians in the stipulations of the Conventions of Geneva and the Hague Tribunal. This instruction ought to be organized in the faculties of medicine all over the world, so that physicians will be informed about the Red Cross.

The medical faculty of Havana has taken the oath which represents a codification of the International Medical Law, to avoid a recurrence of exactions of the war of 1940 to 1945 which were condemned at the trials of Nuremberg. The faculty of medicine of Havana is of the opinion that the course in medical ethics should include the explanation of the International Medical Code.

### MAXILLOFACIAL WOUNDS

Following up the report presented in Mexico, Professor Sanvenero-Rosselli of Milan presented a well documented report on the treatment of maxillofacial wounds, illustrated with numerous photographs.

### AUTONOMY OF MEDICAL SERVICES

The medical corps of the armies and all the professional medical activities ought to be completely autonomous to permit efficient function. Col. H. Glorieux of the medical corp discussed the grave dangers involved in the subordination of the military medical corps to the authorities of the general staffs of the combatant armies. Certain health services play a completely autonomous role, and the studies which have been made since the war of 1914 and 1918 in France have shown how this autonomous status is necessary to insure smooth functioning of the service to the wounded.

### DIVERSE ACTIVITIES OF MEDICAL SERVICES

The military activities of the Mexican and Cuban health services (Colonel Suarez Torres and Hugo Ascanio Marcos) were presented, showing the organization of diverse hospital, nurse and health services of the troops in the Cuban and Mexican armies. A special report on the prevention and treatment of pterygium in the Cuban army by the commander of the medical corps, Manuel Anton, held the attention of the listeners. The campaign against tuberculosis in armies was made the object of a thorough international inquiry, which was presented by Major Greppin of the medical corps of the Swiss army. This inquiry seems to indicate that the improvement in the campaign against tuberculosis in the army depends on that of the entire country and on the collaboration between the military and civil systems. General Heinonen of the medical corps of Finland discussed the question of the rehabilitation of the disabled.

The stay at Havana was rendered interesting and varied by the collaboration of various members of the health services of the army and the navy and of the police force, whose program included not only the technical organizations of the hospitals but various aspects of Cuban life.

## BRAZIL

*(From Our Regular Correspondent)*

SÃO PAULO, Dec. 5, 1949.

### Clinical Aspects of Bronchiogenic Carcinoma

The need for a single classification for both the morphologic and clinical aspects of bronchiogenic carcinoma is emphasized by Dr. Euryclides de Jesus Zerbino of the Medical School of the University of São Paulo. The classification into three fundamental types, small cell carcinoma, adenocarcinoma and squamous cell carcinoma, is considered satisfactory from anatomic, clinical, radiologic, bronchoscopic and surgical aspects. The small cell microscopic distinction is possible. Such tumors are sensitive to irradiation therapy, but their surgical removal is always impossible. The adenocarcinoma is a tumor of the periphery of the lung with early symptoms. As the structures of the hilus are not disturbed much, pneumectomy is possible in many instances. The squamous cell carcinoma also gives early symptoms and has a slow evolution, permitting operation in a high percentage of cases.

Endoscopic observations also show the differences between the three types according to their localization in bronchi of different sizes. Attention is called by Dr. Zerbino to the dissemination through the bronchic, hematic and lymphatic paths and by continuity with surrounding tissues. These conclusions are based on the observation of 22 patients examined in the last two years. Seven of these patients had clinical signs of inoperability; 8 were subjected to a thoracotomy, but it was impossible to perform a pneumonectomy because of the existence of mediastinal metastasis. Pneumonectomies were performed on the last 7 patients, some of them having their mediastinal ganglions extracted. Of these 7 patients, 3 died three days after the operation, 1 died one year later and 3 were still alive five, ten and thirteen months, respectively, after operation.

### Clinical Importance of Rh Factor

Drs. Ruy Faria and Osvaldo Bruno, of the Municipal Hospital of São Paulo, pointed out that routine determination of the blood group and the Rh factor in the pregnant woman is of utmost clinical and scientific interest. This determination leads to a careful study of the immunobiologic trends of pregnancy and should prevent most serious transfusion accidents during pregnancy, fertility being protected in future pregnancies. According to Drs. Ruy Faria and Osvaldo Bruno, in the determination of the Rh factor Chown's method should be adopted, as it is simple, economical, rapid and sensitive and because it also permits seeking Rh antibodies in maternal serum. Reading of the results by Chown's method should not be a simple static observation of the capillary tubes but a dynamic reading, after a soft and delicate tilting of the extremities of the tubes upward and downward, as is done when mixing serum and cells.

The incidence of the four fundamental blood groups and the Rh factor in the unselected group of pregnant women in the study by Drs. Faria and Bruno agrees with that found in other countries, the Rh factor and agglutinogen B being much more frequent among Negro women. The frequent incidence of nulliparity, primiparity and secundiparity in their series may explain the absence of congenital hemolytic disease in the offspring. Natal and neonatal mortality and prematurity were more frequent in the offspring of Rh-negative women than in those who were Rh positive. Early spontaneous abortions were of almost the same frequency among the Rh-positive (14.7 per cent) and Rh-negative (12.5 per cent) subjects. In conclusion, Drs. Faria and Bruno said that simple finding of the binomial expression "An Rh-positive father plus an Rh-positive mother" does not mean danger to the life of the fetus, as congenital hemolytic disease is rarely observed, even in that circumstance.

# Correspondence

## ANTIBIOTICS AND BLOOD COAGULATION

*To the Editor:*—A short current comment appeared in THE JOURNAL (**141**: 924 [Nov. 26] 1949) dealing with the relation of antibiotics to the coagulation of the blood. It stated that the authors of at least one of the three cited papers had expressed the belief that "the definite shortening of the clotting time at the height of antibiotic therapy is of practical clinical interest."

I agree that such a decrease in the clotting time would be of practical clinical interest if it were supported by controlled and statistically reliable data. I would like to point out an extraordinary but nevertheless highly important turn that this subject has taken. In the *New York Times* of Oct. 12, 1949, John N. Popham, in his report of the third session of the Thirteenth Congress of the International Society of Surgery, cites Dr. Alton Ochsner as saying, "The increased incidence of thrombo-embolism and the increased number of fatal cases from pulmonary embolism is probably due to the increased coagulability of the blood resulting from the almost routine administration of antibiotics to all hospital patients." A little later in his news report Mr. Popham quotes Dr. Ochsner as reinforcing this thesis by citing experiments "which demonstrated that patients receiving penicillin injections exhibited increased coagulability of their blood" and that "aureomycin, when administered to patients and to animals, caused a definite shortening of the blood coagulation time."

For some time prior to Nov. 16, 1949, the medical profession in Baltimore waged a vigorous campaign to persuade the Board of Estimates of the City of Baltimore to amend their contract with the local Society for Prevention of Cruelty to Animals to permit the two local medical schools to receive from that organization a certain number of stray dogs which otherwise would be put to death. This action of the medical schools culminated in a public hearing before the Board of Estimates on November 16, which was attended by several thousand persons. The antivivisectionists were there in force, together with their leaders from over the country. The *Evening Sun*, Baltimore, for Nov. 16, 1949, reported some statements made by Mrs. Bennett Champ Clark. "'Penicillin,' Mrs. Clark declared, 'is now known to be the greatest cause of postoperative death. Many people die of it who might never have died. I myself have no doctor. You all might be as well as I am if you followed natural law. Every few years,' she continued, 'the doctors reverse every finding they have made. Meanwhile they are cutting up thousands of innocent dogs.'" Mrs. Clark stated that she based this part of her remarks on a report which she had seen in the *New York Times*. I will hasten to say at this point that one must not be critical of the papers presented at that session or of the newsmen who reported on them. It was unfortunate that the wrong emphasis was placed on certain observations. What are the facts of the case for antibiotics decreasing clotting time and of such a phenomenon, if true, of having any practical importance? The facts are not too clear.—In relation to the experimental observations, at least as far as aureomycin is concerned, they are contradictory. While Macht and Farkas (*Science* **110**: 305, 1949) report increased coagulability, Harned and his co-workers (*Ann. New York Acad. Sc.* **51**: 182, 1948) seem to have demonstrated definitely in dogs that the administration of aureomycin produces no significant change in the clotting time of the blood. This was confirmed in human beings by Ross and his co-workers (*Clin. Proc. Child. Hosp.* **4**: 315, 1948). No one will question Dr. Ochsner's clinical observations, but one can speculate on other factors which might have played a role in the increased incidence of thromboembolism which he observed. We know that since World War II there has been an enormous increase in intravenous therapy and

manipulation. We know that prolonged and complicated operative procedures are much more common. We know that it is now possible to perform extensive operative procedures in patients of the older age group with relative immediate safety. We also know that reports of thromboembolism in medical patients who receive antibiotics are not more frequent. With these contradictions apparent and with the knowledge that inferences as to the causes of thromboembolism are being utilized by the antivivisectionists for their own purposes, is it not desirable that this subject be carefully studied by the surgeons of this country in order that unassailable data may be obtained on this point? It would seem to be a matter of first importance.

PERRIN H. LONG, M.D., Baltimore.

# Medical Examinations and Licensure

## COMING EXAMINATIONS AND MEETINGS

### NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS. *Part III.* Boston, Chicago and New York, January. *Parts I and II,* Feb. 13-15. Centers where there are approved medical schools and five or more candidates. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th Street, Philadelphia 2.

### EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations. July 21. *Oral.* Philadelphia, April 23-27, Chicago, Oct. 8-11. Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written.* Various locations, Feb. 16. *Oral.* Washington, April 7-9. Sec., Dr. George M. Lewis, 66 East 66th Street, New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Chicago, Feb. 8-10. Boston, April 13-15. San Francisco, June 21-23. The oral examinations in the subspecialties will be held at the same time and places. Final date for filing applications for all examinations is Jan. 1. Asst. Sec., Dr. William A. Werrell, 1 West Main Street, Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 3. Sec., Dr. W. J. German, 789 Howard Ave., New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC. *Written and Reviews of Case Histories. Part I.* Various Centers. Feb. 3. *Oral Part II.* Atlantic City, May 21-28. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 1951. Final date for filing applications is July 1, 1950. *Practical.* Boston, May 22-26; Chicago, Oct. 2-6; West Coast, Jan. 1951. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY. *Part II,* New York City, Feb. 9-10. Sec. Treas., Dr. Harold A. Sofield, Room 1856, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* San Francisco, May. Chicago, October. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Written.* Various locations. Jan. 12. *Oral.* Richmond, Va., Feb. 10-12.; Philadelphia, March 31-April 2; San Francisco, June 23-25. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral.* May-June. Sec., Dr. Louis T. Byars, 4647 Pershing Avenue, St. Louis, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: *Oral and Clinical.* Chicago, Feb. 7-8. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe Street, Baltimore 5, Md.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Spring Examination. Date and location of examination to be announced later. Final date for filing applications is Feb. 1. Sec., Dr. F. J. Braceland, 102-110 Second Ave. S.W., Rochester, Minnesota.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, week of June 18. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: *Oral and Clinical.* Chicago, Feb. 11-15. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 21.

BOARD OF THORACIC SURGERY: *Written.* Various locations. Jan. 16. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

### BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 27-29. Sec., Dr. D. G. Gill, 519 Dexter Avenue, Montgomery.

ALASKA: * Juneau, March 7. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARIZONA: * *Examination.* Phoenix, Jan. 17-18. *Reciprocity.* Phoenix, Jan. 21. Sec., Dr. J. H. Patterson, 316 W. McDowell Road, Phoenix.

ARKANSAS: * *Examination.* Little Rock, June 8-9. Sec., Dr. Joe Verser, Harrisburg. *Eclectic.* Little Rock, June 8-9. Sec., Dr. Clarence H. Young, 1415 Main Street, Little Rock.

CALIFORNIA: *Examination, Written.* Los Angeles, Feb. 27-March 2; San Francisco, June 19-22; Los Angeles, Aug. 21-24; Sacramento, Oct. 16-19. *Examination, Oral and Clinical, for Foreign Medical School Graduates.* Los Angeles, Feb. 26; San Francisco, June 18; Los Angeles, Aug. 20; San Francisco, Nov. 12. *Reciprocity, Oral Examination.* Los Angeles, Jan. 21; Los Angeles, Feb. 25; San Francisco, June 17; Los Angeles, Aug. 19; San Francisco, Nov. 11. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

CONNECTICUT: * *Examination.* Hartford, March 14-15. Secretary to the Board, Dr. Creighton Barker, 160 St. Ronan Street, New Haven. *Homeopathic.* Derby, March 9-10. Sec., Dr. Donald A. Davis, 38 Elizabeth Street, Derby.

DELAWARE: *Examination.* Dover, Jan. 10-12. *Reciprocity.* Dover, Jan. 19. Sec., Dr. J. S. McDaniel, 229 State Street, Dover.

FLORIDA: Jacksonville, June 25-27. Sec., Dr. Frank D. Gray, 12 N. Rosalind Avenue, Orlando.

GEORGIA: *Examination.* Atlanta and Augusta, June. *Endorsement.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: *Endorsement.* Agana, last Friday of each month. Sec., Capt. C. K. Youngkin, Dept. of Public Health, Guam, % F.P.O., San Francisco.

HAWAII: *Examination.* Honolulu, Jan. 9-12. Sec., Dr. I. L. Tilden, 881 S. Hotel St., Honolulu.

IDAHO: Boise, Jan. 9. Exec. Sec., Mr. Armand L. Bird, 305 Sun Building, Boise.

ILLINOIS: Chicago, Jan. 10-12. Superintendent of Registration, Mr. Charles F. Kervin, Capitol Building, Springfield.

INDIANA: *Examination.* Indianapolis, June. Sec., Dr. Paul R. Tindall, 1138 K. of P. Bldg., Indianapolis.

MAINE: Portland, March 14-15. Sec., Dr. Adam P. Leighton, 192 State Street, Portland.

MASSACHUSETTS: *Examination.* Boston, March 14-17. Sec., Dr. George L. Schadt, 413 E. State House, Boston.

MINNESOTA: * Minneapolis, Jan. 17-19. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Building, St. Paul 2.

MISSOURI: *Examination.* Jefferson City, Feb. 9-11. *Reciprocity,* Feb. 4. Exec. Sec., Mr. John A. Hailey, Box 14, State Capitol Building, Jefferson City.

MONTANA: Helena, April 3-5. Sec., Dr. Otto G. Klein, First National Bank Building, Helena.

NEVADA: Carson City, May 1. Sec., Dr. George H. Ross, 112 Curry Street, Carson City.

NEW HAMPSHIRE: Concord, March 8-9. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 20-23. Sec., Dr. E. S. Hallinger, 28 West State Street, Trenton.

NEW MEXICO: * Santa Fe, April 10-11. Sec., Dr. Charles J. McGoey, Coronado Building, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 31-Feb. 3. Sec., Dr. Jacob L. Lochner, 23 S. Pearl Street, Albany 7.

NORTH CAROLINA: *Endorsement.* Raleigh, Jan. 23. Sec., Dr. Ivan Procter, 226 Hillsboro St., Raleigh.

OKLAHOMA: * *Examination.* Oklahoma City, June 7-8. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

PENNSYLVANIA: *Examination.* Philadelphia or Harrisburg, Jan. 23-25. Acting Sec., Mrs. Marguerite G. Steiner, 351 Education Building, Harrisburg.

PUERTO RICO: *Examination.* Santurce, March 7. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

SOUTH CAROLINA: *Examination.* Columbia, June 26-29. *Reciprocity.* First Monday of each month. Sec., Dr. N. B. Heyward, 1329 Blanding Street, Columbia.

SOUTH DAKOTA: * Sioux Falls, Jan. 17. Sec., Dr. C. E. Sherwood, 300 First National Bank Building, Sioux Falls.

UTAH. *Examination.* Salt Lake City, June. Dir., Dr. Frank E. Lees, 324 State Capitol Building, Salt Lake City.

VIRGINIA: *Examination.* Richmond, June 23-24. *Endorsement.* Richmond, June 22. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WASHINGTON: * Seattle, Jan. 23-25. Director, Department of Licenses. Mr. Edward C. Dohm, Olympia.

WISCONSIN: * *Examination.* Madison, Jan. 10-12. Sec., Dr. C. A. Dawson, River Falls.

WYOMING: Cheyenne, Feb. 6. Sec., Dr. Franklin D. Yoder, State Capitol, Cheyenne.

* Basic Science Certificate required.

### BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, May 9. Sec., Mr. L. E. Gebauer, 1002 Donaghey Building, Little Rock.

CONNECTICUT: *Examination.* New Haven, Feb. 11. Address: State Board of Healing Arts, 110 Whitney Avenue, New Haven 10.

DISTRICT OF COLUMBIA: Washington, April 17-18. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Building, Washington.

FLORIDA: *Examination.* June 3. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

IOWA: Des Moines, Jan. 10. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids, Iowa.

MICHIGAN: *Examination.* Ann Arbor and Detroit, Jan. 13-14. Sec., Miss Eloise LeBeau, 101 N. Walnut Street, Lansing.

NEBRASKA: *Examination.* Omaha, Jan. 10-11. Director, Bureau of Examining Boards, Mr. Oscar F. Humble, Room 1009, State Capitol Building, Lincoln 9.

RHODE ISLAND: *Examination.* Providence, Feb. 8-9. Chief, Division of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Building, Providence.

OKLAHOMA: *Examination.* Oklahoma City, April 11. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.

TEXAS: *Examination.* Austin, Jan. 20-21 and April 21-22. Sec., Brother Raphael Wilson, 306 Nalle Building, Austin.

WASHINGTON. Seattle, Jan. 18-19. Sec., Department of Licenses, Mr. Edward C. Dohm, Olympia.

# Bureau of Legal Medicine and Legislation

## MEDICOLEGAL ABSTRACTS

**Drunkenness: Admissibility in Evidence of Results of Chemical Tests.**—The defendant was convicted of drunken driving and, from an order denying him a new trial, he appealed to the superior court of New Jersey, appellate division.

Settled medical opinion, said the court, apparently is that any person is unfit to drive when the concentration of alcohol in his blood is at or in excess of 0.15 per cent. When the concentration is less than this, the person may or may not be unfit to drive, depending on individual characteristics and reaction to alcohol. The city physician determined the concentration in the defendant's blood to be over 0.16 per cent and, solely on this finding, testified that defendant was unfit to drive at the time of his arrest.

It appears from the statement of the case that the trial court would have acquitted the defendant except for the evidence produced by a device known as the Harger breath test or drunkometer, on which evidence the city physician predicated his testimony as to the alcohol concentration in the defendant's blood.

The test made by the physician in this case was not a blood analysis but a breath test on the Harger drunkometer. The breath of the person tested is captured in a balloon by his voluntary inflation of it. The breath is then released into a tube in which a color change appears when 0.169 mg. of alcohol has been absorbed by the chemicals in it. Simultaneously the carbon dioxide from the breath passing through the system is absorbed in a tube containing sodium hydrate asbestos absorbent (ascarite®). The weight of the absorbed carbon dioxide represents 5.5 per cent of the weight of the breath from which the stated quantity of alcohol is absorbed. Thus the breath alcohol concentration is arrived at by simple arithmetic when the weight of the absorbed carbon dioxide is known.

The key step in the process, the court continued, is the determination of the weight of the absorbed carbon dioxide, and this is done by weighing the tube containing the carbon dioxide absorbent before and after it absorbs the carbon dioxide. The difference in weight is so minute that its detection requires the use of a scale of great sensitivity, "an analytic balance, to a fine degree, down to 0.1 mg.," was the testimony of the state's expert witness. One ounce avoirdupois is the equivalent of 28,350 mg. A scale sensitive to 0.1 mg. must be capable of resolving a weight change of that part of an ounce expressed by the fraction 1/283,500.

The physician testified that he conducted the test in the "approved" manner by using a pharmacist's scale at a local drug store, but he did not otherwise describe this scale. He seems also to have exhibited at the trial a pamphlet of instructions outlining the Harger test, in which was a photograph of an analytic balance. His testimony was completed on May 21, 1948, at which time the trial judge reserved a ruling as to its admissibility pending the production of expert testimony on the Harger device itself. This was received July 29, 1948. The expert several times in the course of his testimony emphasized that the weights of the tube containing the carbon dioxide absorbent before and after absorption of the carbon dioxide must be determined "to a very accurate degree" "on an analytic balance"; "to complete this test we must have an analytic balance available"; "it is not furnished as any part of the (Harger) apparatus."

The defendant's council discovered after the judgment of conviction that the druggist's scale used by the physician was not an analytic balance but of torsion balance design. The state conceded in the oral argument on the appeal that torsion balance was used. Its sensitivity does not appear, but it seems that commercially available pharmaceutical torsion balances are not sensitive below 2 mg. Such a scale is capable of resolving a weight change of only that part of an ounce which is expressed by the fraction 1/14,175. An analytic balance sensitive to 0.1 mg. has twenty times more resolving power.

The defendant moved for a new trial, which was denied. Motions for new trials for newly discovered evidence, said the appellate division, are not favored and are properly entertained with caution by trial courts, and the elements which must coalesce to entitle a party to a new trial for newly discovered evidence are well known and readily defined. These are (1) that the new evidence must be material to the issue and not merely cumulative nor impeaching nor contradictory; (2) that it has in fact been discovered since the former trial and could not have been discovered before such trial by the exercise of due diligence, and (3) that it would probably change the result if the new trial were granted.

The trial judge was of the opinion that element (2) was lacking because, he concluded, the newly discovered evidence was of such character that reasonable diligence would have enabled the defendant to supply the evidence before the close of the trial. We think, said the court on appeal, that the defendant cannot be charged with lack of due diligence in the circumstances confronting him here. The Harger test is rooted in a technology seemingly not fully understood at this time by any except the technicians who developed it and certainly having flavor of the esoteric to the uninitiated. Even the city physician could perform it only with the aid of a training manual describing the technic and the directions for weighing. Perhaps persons trained in the use of laboratory equipment might be expected to recognize, when laymen might not, the importance of the difference in sensitivity between torsion and analytic balances; still the physician, a competent professional man, seems not to have appreciated the absolute necessity for the use of an analytic balance. That requisite became clear only when, because of the trial court's own doubts as to the validity of the device, the state over two months later produced an expert from the Indiana group who developed the Harger instrument. The impression created by the physician's testimony, taken so much earlier, that he had performed the test in the "approved" manner, was that he had used an analytic balance of the type depicted in the training manual. Justice would be denied the defendant if he were charged with culpable neglect on these facts. Accordingly the judgment of the trial court was reversed and the case was remanded for a new trial.—*State v. Hunter, 68 A. (2d) 274 (N. J., 1949).*

# Medical Motion Pictures

## FILM REVIEWS

**Atomic Medical Cases, Japan—World War II, (PMF 5143). 16 mm., black and white, sound, showing time thirty-seven minutes. Photographed originally in 1945 by the Japanese in the areas of Hiroshima and Nagasaki following the Atomic Bomb Explosions. Condensed version released in 1949 by the United States Army. Procurable on loan from the Army Surgeon of the Army area in which the request originates.**

The film consists of documentary evidence brought on by the atomic explosions at Hiroshima and Nagasaki in 1945. The medical problems measured in terms of distance from the center of the explosion are well shown. The immediate dangers to the central area are shown not only by destruction of buildings and human lives but also by explosion and fire which follow such catastrophies. The greater the distance from the explosion, the less the injuries. The instantaneous catastrophies that occur are well demonstrated by the area of the human body which is exposed to the site of injection. Pathologic specimens and studies of fatal cases are shown in microscopic section. The spontaneous chaos which follows such an explosion is well presented by the attempt to use the remaining doctors, nurses and Red Cross services to the greatest advantage in carrying out first aid and medical care.

It should be of definite interest to members of county and state medical societies, medical students and organizations which are mobilized to care for disaster work. This film opens the minds of physicians to problems which they may face in the event of bombing; however, it is not an instructional film since it shows only the parts of the body exposed to the bomb and does not illustrate the treatment in these cases.

This picture was photographed under adverse conditions; therefore the quality is fair to good. The narration is clear.

# Current Medical Literature

## AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

### American Heart Journal, St. Louis

**38**:161-320 (Aug.) 1949

Certain Aspects of Nature and Treatment of Oligemic Shock. I. H. Page.—p. 161.
Ventricular Fibrillation Induced by Cold. H. E. Hoff and H. Stansfield. —p. 193.
Pathology of Intrapulmonary Arteries and Arterioles in Coarctation of the Aorta Associated with Patent Ductus Arteriosus. J. E. Edwards, J. M. Douglas, H. B. Burchell and N. A. Christensen.—p. 205.
Water Tolerance of Hypertensive Patient. Its Relation to Operability. G. De Takats and E. F. Fowler.—p. 234.
Studies on Peripheral Circulation and Epinephrine Sensitization Following Sympathectomy. R. A. Deterling Jr. and H. E. Essex.—p. 248.
Differentiation of Changes in the Q-T Interval in Hypocalcemia and Hypopotassemia. A. C. Ernstene and W. L. Proudfit.—p. 260.
Ventricular Complex in Right Ventricular Hypertrophy as Obtained by Unipolar Precordial and Limb Leads. M. Sokolow and T. P. Lyon. —p. 273.

### American Journal of Clinical Pathology, Baltimore

**19**:701-800 (Aug.) 1949

Adhesiveness of Blood Platelets in Thromboembolism and Hemorrhagic Disorders. I. Measurement of Platelet Adhesiveness by Glass-Wool Filter. S. E. Moolten and L. Vroman.—p. 701.
Quantitative Correlation of Morphologic Liver Changes and Clinical Tests. H. Popper, F. Steigmann and P. B. Szanto.—p. 710.
*Sarcoidosis: Clinicopathologic Review of Three Hundred Cases, Including Twenty-Two Autopsies. W. Ricker and M. Clark.—p. 725.
Hashimoto's and Riedel's Strumas and Lymphadenoid Goiter. S. M. Rabson and J. E. Arata.—p. 750.
*Cytologic Diagnosis of Bronchogenic Carcinoma. L. B. Woolner and J. R. McDonald.—p. 765.
*Progression from "Precancer" Stage to Early Carcinoma of Cervix Within One Year: Combined Cytologic and Histologic Study with Report of Case. J. E. Ayre and W. B. Ayre.—p. 770.
Further Studies on the rh' Factor. A. S. Wiener, L. J. Unger and C. A. Mazzarino.—p. 779.
Abnormal Agglutinability of Red Cells in Pyogenic Infections: Report of Two Cases. G. Engleson and R. Grubb.—p. 782.

**Sarcoidosis.**—Ricker and Clark review 300 cases of sarcoidosis from the files of the Army Institute of Pathology. In 278 patients who had been hospitalized because of sarcoidosis or for other reasons, a definite diagnosis of sarcoidosis was made during life from biopsy or from tissue removed during operation for other causes. The presence of sarcoidosis was either detected or confirmed at necropsy in 22 additional cases. The disease reached peak occurrence in the age group between 20 and 24 years. It occurred 17 times as often among Negroes as among white men in the Army. Of the 258 patients who presented symptoms on admission to the hospital, 221 (86 per cent) had enlarged lymph nodes, 51 (20 per cent) had cough, 48 (19 per cent) weight loss, 40 (16 per cent) skin manifestations, 38 (15 per cent) low grade fever, 26 (10 per cent) malaise and 26 (10 per cent) weakness. In the entire group of 300 patients the organs involved in order of frequency were lymph nodes, lungs, skin, bone, eyes, liver and spleen. Over two thirds of the patients were admitted to hospitals within six months after they first noticed symptoms. Roentgenologic examination showed mediastinal widening in 76 per cent of patients examined, while small bone involvement was seen in 36 per cent of the patients who had roentgenologic examinations of the extremities. Tuberculin tests were made in 88 patients, and results were negative in 85. The sedimentation rate was determined in 52 patients and was elevated in 32. The total plasma protein was determined in 40 patients and hyperproteinemia (8 Gm. or more per hundred cubic centimeters of blood) was present in one third of these patients. Sixty-seven patients answering follow-up questionnaires reported recurrence of symptoms consistent with sarcoidosis. In 14 of the 22 cases in which the diagnosis was made at necropsy, sarcoidosis was unsuspected until then, and in only 3 was death unequivocally due to sarcoidosis. Three of the 22 patients had associated sarcoidosis and tuberculosis, and an additional 2 of the 22 showed abacterial caseating lesions of the adrenal glands with clinical Addison's disease.

**Cytology in Bronchial Carcinoma.**—Woolner and McDonald diagnosed carcinoma on cytologic examination of sputum or bronchial secretions in 300 patients. This total was divided into two groups, the first 150 cases for investigation of the method, and the second 150 cases for evaluation of the method as a routine procedure in the diagnosis of thoracic diseases. There were 3 false positive results in the first series and 1 in the second series. In a group of 588 patients with miscellaneous diseases of the thorax, for whom routine cytologic examination of sputum or bronchial secretions was carried out, bronchogenic carcinoma was proved or suspected in 147. In 100 patients, 68 per cent of the 147, the lesions were detected by cytologic examination of sputum or bronchial secretions.

**Cytology in Early Cervical Carcinoma.**—The Ayres report a multipara aged 32, in whom abnormal, so-called "precancer" or "nearo-cancer" cell types in epithelial smears from the uterine cervix were studied at frequent intervals during one year. A total dose of 480 mg. of progesterone and a total dose of 1,500 mg. of diethylstilbestrol were administered intramuscularly three months during this time, in an effort to promote normal cell development, without success. In abnormal cells scraped from the squamous marginal area of the cervix, using a modification of Papanicolaou's technic, the authors observed morphologic progressive change to a malignant type, after which biopsies of cervical tissue confirmed the presence of carcinoma in an early infiltrative stage. Clinically, the cervix remained normal in appearance throughout the period of observation. The cervical cell-scraping modification of the Papanicolaou technic constitutes a useful and highly sensitive method of identifying the early formative stage of cervical cancer.

### American Journal of Public Health, New York

**39**:969-1090 (Aug.) 1949. **Partial Index**

Psychological Factors in Atomic Warfare. J. P. Cooney.—p. 969.
Water-Borne Diseases. I. H. Borts.—p. 974.
The Caries Problem of School Child. K. A. Easlick.—p. 983.
Adjustment of School Program for Physically Handicapped Child. S. M. Wishik and R. P. Mackie.—p. 992.
Gathering and Evaluating Accident Data with Respect to Farm People and Farm Workers. T. C. M. Robinson.—p. 999.
Development of Educational Program on Sanitation in a Typical Food Industry—Baking Industry. E. L. Holmes.—p. 1004.
Rhode Island Cash Sickness Compensation Program. T. H. Bride. —p. 1011.
Tuberculosis in School for Mental Defectives. R. E. Plunkett, J. Katz, M. E. Thompson and R. R. Donk.—p. 1016.
Trimming the Tuberculosis Register. J. H. Korns.—p. 1021.
Poisoning Due to Ingestion of Wax Crayons. H. Brieger.—p. 1023.

### Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

**62**:1-158 (July) 1949

Cushing's Disease—Pituitary Basophilism; Caldwell Lecture, 1947. M. C. Sosman.—p. 1.
Development of Tautography and Advantages of Automatization in Cardiovascular Angiography. W. G. Scott and S. Moore.—p. 33.
Pulsating Exophthalmos Due to Defective Development of Sphenoid Bone. E. G. Robertson.—p. 44.
Solitary Tumors of Chest: Differential Diagnosis in 50 Proved Cases. R. K. Arbuckle.—p. 52.
Bronchial Peristalsis. F. G. Fleischner.—p. 65.
*Double Contrast Roentgenograms of Stomach; Additional Aid in Diagnosis. E. L. Pirkey.—p. 70.
Relation of Therapeutic Radiology to Clinical Medicine. A. U. Desjardins. —p. 75.
Pyelography by Rapid Injection: Description of Improved Method and Results in 200 Cases. L. J. Friedman, H. Lobsenz and R. Jauernig. —p. 84.
Physical Characteristics of Soft Roentgen Rays. E. D. Trout and R. M. Gager.—p. 91.

**Double Contrast Roentgenograms of Stomach.**—To improve the accuracy in the diagnosis of lesions of the stomach, Pirkey used an air-filled balloon in the barium-containing stomach. After the customary roentgenoscopic examination of the barium-filled stomach, the patient swallows a stomach tube (Rehfuss or Levine) with a latex condom tied tightly proximal

to all the holes. A hand bulb from a blood pressure apparatus is attached to the outside end of the tube and the balloon is inflated under roentgenoscopic control to any desired degree. This causes a varying degree of gastric dilatation and makes it possible in most subjects to palpate the lower end of the balloon in the pyloric antrum, thereby giving transmitted pulsations to the fundus. Tilting of the patient gives control of the amount of barium in the fundus or prepylorus. The maximum pressure used did not exceed 20 mm. of mercury. None of the patients complained of pain. One patient attempted to vomit but without success. Two balloons ruptured while in the stomach, but the patient was not aware of what had occurred. Two roentgenograms are taken in the right anterior oblique position, which allows the balloon to float into the fundus area and the barium sulfate to descend into the prepylorus. The other two roentgenograms are taken in the left posterior oblique position, which gives the opposite effect, in that the balloon floats into the prepylorus and the barium enters the fundus. The roentgenograms are all taken with the patient horizontal. This method obtains what amounts to internal palpation of the stomach plus excellent double contrast roentgenograms of almost any area of the stomach. It has been of value in reducing the number of false positive diagnoses, particularly in the fundus, where external palpation is not possible.

## American Journal of Surgery, New York

**78**:143-278 (Aug.) 1949

New Horizons in Surgical Management of Carcinoma of the Prostate Gland. R. Gutierrez.—p. 147.
Use of Fibrin Film in Repair of Experimentally Produced Hernias. G. N. Lassar and B. Hulbert.—p. 170.
Cancer of the Gallbladder: Report of Five-Year Cure of Anaplastic Carcinoma with Metastases. R. J. Booher and G. T. Pack.—p. 175.
Minimal Saddle-Block Anesthesia for Vaginal Delivery. L. T. Dorgan, H. S. McGaughey and L. D. Litton.—p. 181.
Internal Fixation of Fractures of the Femoral Neck. R. K. J. Luomanen and J. F. Prudden.—p. 189.
Malignant Tumors of the Thyroid Gland: Diagnosis, Management and End Results. F. Teller.—p. 199.
Low Back Pain and Sciatica. C. J. Wagner.—p. 203.
Thiouracil and Surgery of the Thyroid Gland. T. J. Anglem and F. R. Kenney.—p. 210.
The Perforated Appendix. H. A. Burnett.—p. 213.
Possible Mechanism of Postcoronary Shoulder Pain. B. D. Judovich, W. Bates and M. S. Jacobs.—p. 216.
Anesthesia for Extremity Amputations: Statistical Review of 185 Major Amputation Cases. M. P. Peters, G. R. Broberg and G. A. Light.—p. 220.
Prevention of Postoperative Pulmonary Complications. E. M. Colvin and F. T. Wallace.—p. 226.
Oxytocics in Labor. A. Golden.—p. 229.

## Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

**33**:297-408 (July) 1949

Duration of Acquired Immunity in Experimental Syphilis. H. J. Magnuson, B. J. Rosenau and J. W. Clark Jr.—p. 297.
Studies of Life and Motility of Treponema Pallidum in Fertile Hens' Eggs. R. J. Rowe and A. C. Curtis.—p. 303.
Susceptibility of Various Strains of Mice to Experimental Syphilis. H. J. Magnuson, B. J. Rosenau and J. W. Clark Jr.—p. 308.
Observations on Growth of Nonpathogenic Nichols Strain of Treponema Pallidum in Embryonated Chick Egg Under Anaerobic Conditions. V. D. Newcomer and M. Haanes.—p. 318.
Relationship of Early Clinical Failure to Serologic Response in Penicillin-Treated Early Syphilis. M. T. Hockenga, M. S. Buerk and R. V. Rider.—p. 323.
Reinfection in Syphilis. G. E. Peabody and B. Webster.—p. 334.
*Penicillin Treatment of Late Neurosyphilis—One to Five-Year Follow-Up with Special Reference to Clinical Failures. D. Landau, I. Kopp, A. S. Rose and H. C. Solomon.—p. 357.
*Difficulties in Evaluation of Treatment Procedures in Tabes Dorsalis. H. Koteen.—p. 364.
Describing Contact of Venereal Disease. N. J. Fiumara.—p. 380.
Aureomycin in Treatment of Granuloma Inguinale. R. C. V. Robinson, DuM. F. Elmendorf Jr. and H. E. C. Zheutlin.—p. 389.

**Penicillin in Treatment of Neurosyphilis.**—Landau and associates review observations on 446 patients with neurosyphilis who were treated by them over a five year period. During the first sixteen months, penicillin was given intramuscularly, 3,000,000 units over a period of five to fifteen days. Thereafter 6,000,000 units were given in fifteen days. Fever therapy was administered in amounts equivalent to one-half the usually accepted course of therapy, five to seven paroxysms of malaria or twenty hours of artificial fever (above 105 F., rectal). One fourth of the group was given only penicillin; the others also received fever therapy. Fifty-two patients died, but in only 16 of these could death be attributed to the syphilitic process. Seventeen patients were lost from observation. Of the 377 patients that are being followed, two thirds are improved; the remainder are unimproved or unchanged. Analysis of the present clinical status of 233 paretic patients that have been followed for more than a year indicates that the type of psychosis present prior to treatment largely determines the prognosis. Psychoses of the affective type have an excellent prognosis; all of these patients improved although a few required electric shock therapy in addition to the penicillin. Two thirds of the patients in the demented group improved and only one fourth of those with schizophrenia-like symptoms showed improvement. In addition to the type of psychosis, residua of severe organic lesions were decisive factors in the therapeutic failures.

**Evaluation of Treatments in Tabes Dorsalis.**—Koteen emphasizes the extreme variability of the tabetic syndrome and the difficulties inherent in the evaluation of therapy. Even the attitude of the interviewing physician may determine in part the response of the patient concerning interpretation of "improvement." The authors reviewed 403 patients with tabes dorsalis registered at New York Hospital in the Cornell University Syphilis Clinic from 1932 to 1948. They evaluate in detail 49 patients who were treated with penicillin. They found that certain signs and symptoms are not reversible. Pupillary abnormalities, loss of deep pain, position and vibratory sensibilities and trophic lesions do not respond to any form of antisyphilitic therapy, because these lesions are associated with damage to the sensory nerve fibers and the nervous tissue cannot be revitalized. Symptoms of less than two years' duration are more amenable to therapy than those of a longer period; this is especially true of shooting pains and ataxia. Patients who fail to respond to one form of antisyphilitic therapy are less likely to have good results subsequently. Patients who continued to have discomforts after arsenobismuth and malaria therapy obtained little relief from penicillin. Patients who were not aided by one or more courses of penicillin did not do well after fever therapy. The nature and duration of the symptoms and failure in response to previous therapy are more important in the prognosis than is the condition of the cerebrospinal fluid. The results following treatment with penicillin are as satisfactory as those following previously used methods. The use of tryparsamide should be abandoned, not only because therapeutic efficacy has not been proved but because there is danger of optic atrophy.

## American Journal of Tropical Medicine, Baltimore

**29**:435-646 (July) 1949. **Partial Index**

Tropical Disease Problems Among Veterans of World War II. T. T. Mackie and B. Sonnenberg.—p. 443.
Incidence of Trypanosoma Cruzi, Chagas, in Triatoma (Hemiptera, Reduviidae) in Texas. T. D. Sullivan, T. McGregor, R. B. Eads and D. J. Davis.—p. 453.
Inflammatory Reaction to Toxoplasma in Omentum and Peritoneal Fluid of Mouse. J. B. Cross and L. Anigstein.—p. 473.
Plague Among Wild Rodents in Rio Arriba County, New Mexico. V. B. Link.—p. 493.
Epidemic Typhus in Southwestern Arabia. P. W. R. Petrie.—p. 501.
*Sheep and Goats in Epidemiology of Q Fever in Northern California. E. H. Lennette, W. H. Clark and B. H. Dean.—p. 527.
Analyses from Tropical Epidemic of Poliomyelitis Which Occurred in Florida and Cuba in 1946. J. R. Paul, F. Ramirez Corria and D. M. Horstmann.—p. 543.
Invasion of Small Forests by Yellow Fever Virus as Indicated by Immunity in Cebus Monkeys. H. W. Laemmert, T. P. Hughes and O. R. Causey.—p. 555.
Methods of Pinwork Diagnosis. P. C. Beaver.—p. 577.
Treatment of Loa Loa Infections with Hetrazan. H. B. Shookhoff and K. G. Dwork.—p. 589.
Intensive Treatment of Regimen of Vesical Schistosomiasis with Fuadin. J. E. Azar, A. C. Pipkin and G. A. Garabedian.—p. 595.
Tropical Chigger, Eutrombicula Batatas (Linn.) Attacking Man in California. W. H. Doetschman and D. P. Furman.—p. 605.
Principles of Fly Control for Sanitarian. H. I. Scudder.—p. 609.

**Sheep and Goats in Q Fever.**—According to Lennette and his associates the first cases of Q fever in Northern California were uncovered in early March 1948 by means of serologic surveys and by serologic examination of blood specimens sent in by physicians. Field investigations obtained evidence suggesting sheep and goats as possible sources of human infec-

tion. Cases of Q fever in human beings in Northern California appear to be at least as frequently associated with contact with sheep and goats as with cattle. Serologic studies indicate that infection with Rickettsia burneti is much more prevalent in sheep (37.9 per cent) and goats (43.6 per cent) epidemiologically linked with human cases, than in cattle similarly associated with human infections. Serologic surveys of the sheep and cattle population received at slaughter houses indicate that the extent of infection in this group is small; 3.1 per cent of the cows and calves and 3.5 per cent of the sheep examined were found to possess antibodies. Data on goats were too few for analysis. The serologic data indicate that infections in man, sheep and probably goats, are epidemiologically related. That the role of sheep and goats in the epidemiologic of the human disease is important finds additional support in the demonstration that the rickettsia is excreted in the milk of these species. The possibility of air-borne transmission of Q fever is considered.

## Annals of Otol., Rhin. and Laryngology, St. Louis

**58**:323-610 (June) 1949. **Partial Index**

Acoustic and Vestibular Barometry; Air Pressure Effects on Hearing and Equilibrium of Unoperated and Fenestrated Ears. M. F. Jones and F. C. Edmonds Jr.—p. 323.
Early Diagnosis of Primary Carcinoma of Lung. O. E. Anderson. —p. 370.
Transitional Cell Carcinoma of Paranasal Sinuses. L. A. Schall and D. W. Brewer.—p. 381.
Hearing Evaluation by Low Conversational Voice Tests. A. Glorig. —p. 394.
Tuberculosis of Nose Treated with Streptomycin. C. S. Lane.—p. 403.
Operation for Correction of Collapsed Nostrils and Narrowed External Nares. J. J. Conley.—p. 407.
Dust Therapy in Allergy of Ear, Nose and Throat. R. E. Ashley. —p. 417.
Are Any Strictures of Esophagus Due to Diphtheria? U. K. Kiviranta. —p. 429.
Tuberculous Laryngitis and Tracheobronchitis. J. J. O'Keefe.—p. 441.
*Toxic Effect of Streptomycin on the Eighth Cranial Nerve: Histological Investigations. Preliminary Report. K. Berg.—p. 448.

**Toxic Effect of Streptomycin on Eighth Cranial Nerve.**—Berg points out that a disturbance of the vestibular function frequently results when large doses of streptomycin are given over long periods as is the case in tuberculosis. Numerous publications concerning clinical observations and observations on animals show that a vestibular dysfunction is frequently produced after prolonged treatment with large doses, whereas impairment of hearing has seldom been observed. To determine the actual site of the lesion responsible for the vestibular dysfunction and the much rarer impairment of hearing, Berg investigated the toxic effect of streptomycin on the vestibular apparatus of 25 cats. He shows that the primary lesion is localized in the sensory epithelium of the labyrinth. Slight, presumably secondary, changes have been demonstrated in the vestibular ganglion. Degenerative changes of the organ of Corti were found in 1 animal.

## Archives of Dermatology and Syphilology, Chicago

**58**:659-778 (Dec.) 1948

Urticarial Reaction Induced in the Dog by Intravenous Injection of Sorbitol Monolaurate. A. C. Ivy, C. A. Tanturi, R. Hernandez and E. Baroso.—p. 659.
Colloid Milium. H. Hailey.—p. 675.
*Calciferol in Treatment of Cutaneous Tuberculosis. H. E. Michelson and J. R. Haserick.—p. 680.
Some Dermatologic Eponyms. J. B. Haeberlin Jr. and H. F. Garrard. —p. 696.
*Recent Observation on Granuloma Inguinale, with Report on Streptomycin Therapy. C. H. Chen, R. B. Greenblatt and R. B. Dienst.—p. 703.
Erythema Elevatum Diutinum: Report of 3 Cases. R. S. Weiss, Z. K. Cooper and H. R. Gottschalk.—p. 716.
Histopathology of Atopic Dermatitis and Characteristic Atopic Reaction to Patch Test. F. A. Simon and A. J. Miller.—p. 728.
Herxheimer Reactions in Penicillin Treatment of Syphilis in Pregnancy. J. H. Bowen, H. N. Cole, J. R. Driver and others.—p. 735.

**Calciferol in Cutaneous Tuberculosis.**—Twenty-five patients with cutaneous tuberculosis included 7 with lupus vulgaris, 9 with erythema induratum, 4 with papulonecrotic tuberculids and 5 with colliquative tuberculosis. At first viosterol in oil was used; later a solution of calciferol in propylene glycol (drisdol®), especially prepared in a concentrated form of 50,000 units per cubic centimeter, was used. Calciferol is a valuable adjunct in the treatment of cutaneous and nodular tuberculosis. It has exceptional value in the treatment of lupus vulgaris, but its precise mode of action is not known. Calciferol therapy combined with injections of streptomycin is worthy of further trial. The authors found the systemic toxic symptoms to be minimal, but, as a precautionary measure, calciferol was not administered to any patient with arteriosclerosis or with impaired renal function. When toxicity occurred, the earliest sign was nausea, with anorexia and headache the next more frequent signs. In no case in which the patient was ambulatory was it necessary to stop administration of the drug because of toxic symptoms, though a rapid onset of hypercalcemia in 1 case prompted withdrawal. Of 8 bedridden patients, 5 had reactions considered severe enough to discontinue the drug.

**Streptomycin in Granuloma Inguinale.**—Chen and his associates treated 142 patients with laboratory-proved granuloma inguinale. These patients were observed from one to three years. Diagnosis was based on the finding of intramonocytic Donovan bodies. In rare cases (3 in this series) in which Donovan bodies could not be found in tissue smears, biopsy was done and revealed typical intramonocytic organisms. Biopsy also served to determine the possibility of other diseases, such as cancer and syphilis. Fusospirochetosis, if present, was first treated with one or two injections of 300,000 units of penicillin in oil and wax given intramuscularly. Streptomycin was then given intramuscularly in six equally divided doses at four hour intervals. The authors concluded that streptomycin is the most effective agent in granuloma inguinale. The optimal dosage is 4 Gm. per day, given intramuscularly in divided doses, for five to ten days. The ten day course is probably preferable, at least in those cases in which Donovan bodies are still present at the end of a five day course and in cases with extensive lesions.

## Archives of Otolaryngology, Chicago

**50**:115-242 (Aug.) 1949

*Otosclerosis: Theory of Its Origin and Development. J. Lempert and D. Wolff.—p. 115.
*Inhalation of Penicillin and Streptomycin in Office Practice. D. Davis. —p. 156.
Role of Compensatory Hypertrophy and Simple Atrophy in Intranasal Surgery. J. M. Evans.—p. 172.
Study on Range of Usefulness of New Dual Form Intranasal Medicament. B. L. Griesman.—p. 190.
Tympanosympathetic Anesthesia for Tinnitus Aurium and Secondary Otalgia. B. C. Trowbridge.—p. 200.
Uvula and Tonsils. E. Foreschels.—p. 216.

**Otosclerosis: Theory of Origin and Development.**—Lempert and Wolff, in 1945, described histologic studies on the incus and the head and neck of the malleus in 115 cases of ankylosing of the stapedial footplate caused by a proliferating otosclerotic lesion in the region of the oval window. These ossicles had been removed during the fenestra nov-ovalis operation. The authors report microscopic studies on a second series of ossicles removed from 100 patients whose labyrinths were being fenestrated for clinical otosclerosis. The incus, the head and neck of the malleus and occasionally the head and crura of the stapes were included. An outstanding observation was that the blood vessels constantly showed pathologic involvement similar to the involvement of the blood vessels in otosclerotic foci observed within the otic capsule. Since these ossicles were always removed in vivo, they did not undergo postmortem changes. The authors stress that one ossicle may present any one or a combination of pathologic processes. Areas of decalcification were numerous and extensive. Osteofibrosis, osteoporosis, hyperostosis and sclerosis may occur. The cubic volume of the lesion is minute, but because of the strategic location of the alteration the significance of its presence is great. The types of pathologic involvement seen in these ossicles may also be seen within the ossicles in clinically diagnosed otosclerosis observed at necropsy. The lesion is not circumscribed in the ossicles as it is in the otic capsule. This, the authors believe, is due to the anatomic difference in the blood supply. The otic capsule receives its blood supply from six different sources. The ossicles receive their blood supply from one or at most two sources. It is possible in the otic capsule for a circumscribed area supplied by a certain blood vessel undergoing pathologic changes to lie more or less completely surrounded by areas still receiving a normal supply of blood and therefore

maintaining a normal histologic picture. The pathologic changes are a part of the otosclerotic process. The authors believe that the vascular changes preceded the bone changes in the development of otosclerosis. They studied the blood vessels and found that the pathologic changes led in more or less chronologic steps to the various types of bone disease. The initial pathologic changes are within the blood stream. The ages of the patients in this series suggest that senescence probably does not play a part in the pathologic changes.

**Inhalation of Penicillin and Streptomycin in Office Practice.**—Davis points out that inhalation is a simple method of applying drugs to the entire respiratory mucosal tract in sufficient concentration to be effective against bacteria. The drugs most commonly used are penicillin and streptomycin. Bacitracin, hydrogen peroxide, urea peroxide, the sulfonamide compounds, chlorophyll, aminophylline and iodized oil are also used effectively. The apparatus consists of a nebulizer, which connects with a face mask and a rebreathing bag, and a tank of oxygen, which supplies the pressure. Compressed air can be used instead of the oxygen. For sinus treatments, nasal tips and a suction-pressure apparatus are used instead of the face mask and the rebreathing bag. Inhalation treatment is effective in acute or chronic sinusitis, nasopharyngitis, pharyngitis, tonsillitis, laryngitis, bronchitis, bronchiectasis, cough and infectious asthma. Even colds in the head frequently respond to the inhalation of penicillin. In infection of the respiratory tract due to gram-positive organisms, penicillin aerosol alone is effective. If gram-negative organisms are present, streptomycin, alone or combined with penicillin, is used. Inhalation of 150,000 units of penicillin once or twice a day for six days or less is usually sufficient to reduce most acute or subacute conditions. For chronic conditions, such as bronchiectasis or chronic sinusitis, daily treatment may be necessary for thirty days or longer. If streptomycin is used, 0.3 to 0.5 Gm., alone or combined with penicillin, is given. Treatments may be taken at home with any one of the various types of apparatus described. Infants and small children can be treated through a plastic hood tucked around the head and neck.

## Archives of Pathology, Chicago

**48**:105-194 (Aug.) 1949

*Incidence of Fatal Coronary Disease in Nondiabetic and in Diabetic Persons. B. J. Clawson and E. T. Bell.—p. 105.
Primary Alveolar Cell Tumors of Lung. T. C. Laipply and C. I. Fisher.—p. 107.
Arsenical Encephalopathy: Report of Case. R. A. Call and F. D. Gunn.—p. 119.
Effect of Experimental Thiamine Deficiency on Nervous System of Rhesus Monkey. J. F. Rinehart, M. Friedman and L. D. Greenberg.—p. 129.
Pathologic Changes After Partial Hepatectomy with Special Reference to Hepatic Necrosis in Protein-Depleted Rats. F. N. Gurd and H. M. Vars.—p. 140.
Unusual Hamartoma of Lung in Newborn Infant. C. J. Jones.—p. 150.
Absence of Pulmonary Artery: New Classification for Pulmonary Arteries of Anomalous Origin: Report of Case of Absence of Pulmonary Artery with Hypertrophied Bronchial Arteries. L. J. Manhoff Jr. and J. S. Howe.—p. 155.
Radioresistant Cells in Certain Radiosensitive Tissues of Swine Exposed to Atomic Bomb Radiation. J. L. Tullis.—p. 171.
Effect of Tripelennamine Hydrochloride on Acute Inflammation. R. E. Weeks and R. M. Gunnar.—p. 178.
Glioma of Nose: Report of Case of Extranasal Type. J. H. Hill.—p. 183.

**Fatal Coronary Disease in Diabetic and Nondiabetic Persons.**—Clawson and Bell analyzed the postmortem records on file in the department of pathology of the University of Minnesota covering the period 1910 through 1947. The total number was 50,775. There were 49,593 nondiabetic and 1,182 diabetic subjects. They obtained evidence that diabetes accelerates atherosclerosis of the coronary arteries. It has a more pronounced effect in female than in male subjects. About 4 per cent of deaths due to coronary disease in male patients and nearly 14 per cent in female patients are associated with diabetes.

## Arkansas Medical Society Journal, Fort Worth

**46**:45-62 (July) 1949

Hemochromatosis: Report of Case in White Female Without Diabetes. C. T. Chamberlain.—p. 45.
"The Doctor as a Citizen." R. B. Robins.—p. 50.

## Blood, New York

**4**:891-988 (Aug.) 1949

Familial Hypochromic Anemia Associated with Postsplenectomy Erythrocytic Inclusion Bodies. H. Mills and S. P. Lucia.—p. 891.
*Iron Metabolism: Utilization of Intravenous Radioactive Iron. C. A. Finch, J. G. Gibson II, W. C. Peacock and R. G. Fluharty.—p. 905.
Hemolysins in Acquired Hemolytic Anemia: Effect of *p*H on Activity in Vitro of a Serum Hemolysin. J. V. Dacie.—p. 928.
Observations on Influence of Hypophysis and Adrenal Cortex on Blood Platelet Levels. E. Adams.—p. 936.
Effect of Human Plasma Transfusions on Fecal Urobilinogen Excretion in Sickle Cell Anemia. E. Kaplan and S. R. Lewis.—p. 947.
Effect of Quantitative and Qualitative Protein Deficiency on Blood Regeneration. I. White Blood Cells. K. Guggenheim and E. Buechler.—p. 958.
Effect of Quantitative and Qualitative Protein Deficiency on Blood Regeneration. II. Hemoglobin. E. Buechler and K. Guggenheim.—p. 964.
Hypoplastic Anemia Due to Atabrine. A. P. Fishman and J. M. Kinsman.—p. 970.
Influence of Fibrinogen Concentration upon Plasma Prothrombin Time. M. Weiner and S. Shapiro.—p. 977.

**Iron Metabolism.**—Finch and co-workers administered radioiron intravenously to 9 normal persons, to 3 persons with miscellaneous diseases and to 50 patients with various hematologic disorders. When single tracer doses of radioactive iron ($Fe^{55}$ and $Fe^{59}$) are given intravenously, the radioiron rapidly enters the hemoglobin cycle and "tagged" erythrocytes begin to appear in the circulation within twenty-four hours. Thereafter the radioactivity of circulating red cells rises and reaches a plateau in two or three weeks. By determining the percentage utilization of the intravenously administered radioiron for hemoglobin production over this period, certain measurements of internal iron metabolism can be made. With a normal rate of blood production, changes in the percentage of utilization reflect alteration in iron stores. Iron depletion is characterized by more rapid and more complete utilization of radioiron. States of iron excess in hemochromatosis can be identified by their profound depression of radioiron utilization. If storage iron is not greatly altered, the percentage utilization is determined by the function of the erythropoietic tissues. A similar depression of the curve is observed in myelophthisic anemias, in uremia and in infection. The rate of erythropoiesis may be estimated by the slope of the utilization curve. Evidence of abnormal red cell destruction is found in early and abrupt plateau of the utilization curve. A correlation has been made between the radioiron utilization for hemoglobin production and the clinical factors which might be expected to affect iron metabolism in patients with various hematologic disorders.

## Canadian Medical Association Journal, Montreal

**61**:99-204 (Aug.) 1949

Let Us be Practical About the Psychoneuroses. H. R. Brillinger.—p. 99.
Indications for Splenectomy. R. E. McKechnie.—p. 103.
Early and Accurate Diagnosis in Jaundice. M. M. Baird, E. J. Badre, A. Bogoch and I. D. Maxwell.—p. 107.
Congenital Malformation of the Heart. Method for Surgical Treatment of Congenital Pulmonary Stenosis and Atresia: Experimental Study (Preliminary Report). D. E. Ross and D. R. Murphy.—p. 114.
*Carotid Sinus and Coronary Circulation. H. N. Segall, J. Wener and R. Druckman.—p. 118.
Cerebral Changes Related to Anoxia, with Report of Case. A. S. Douglas.—p. 123.
*Essential Brown Induration of the Lungs (Idiopathic Pulmonary Haemosiderosis). N. G. B. McLetchie and G. Colpitts.—p. 129.
Comparison of Intramuscular and Oral Penicillin in Pneumococcic Pneumonia. W. W. G. Maclachlan, M. M. Bracken, M. P. Lynch and W. R. Bailey Jr.—p. 134.
Role of Retropubic Operation in Selective Prostatic Surgery. C. L. Gosse.—p. 138.
*Oesophageal Varices. C. B. Ripstein.—p. 141.
Non-Surgical Abdominal Pain. D. Macdonald.—p. 148.
Rheumatoid Arthritis. D. Robinson.—p. 152.
Clinical Evaluation of Hydryllin and Trimeton (Tripoton) in Allergic Manifestations. B. A. Manace.—p. 156.
Submucous Lipoma of the Colon. J. G. Stapleton.—p. 159.

**Carotid Sinus and Coronary Circulation.**—Segall and co-workers practiced carotid sinus pressure on the right and the left side alternately in 446 patients. One hundred and forty-four of these did not present any evidence of cardiovascular disease; 92 had symptoms of chronic coronary artery disease; 48 had cardiac pain at rest and usually also on exertion without

evidence of myocardial infarction; 16 presented symptoms and signs of recent acute coronary disease and myocardial infarction and 146 had objective signs of myocardial disease. Electrocardiographic recordings were made before the carotid sinus pressure was started, during the carotid sinus pressure, and during the period of recovery from the carotid sinus pressure. None of the 446 patients experienced cardiac pain as the result of the carotid sinus pressure. This does not necessarily indicate that the nerve supply to the coronary arteries is inert. Carotid sinus pressure elicited striking changes in the T waves in the electrocardiogram in 11 patients. The T wave changed from upright to inverted in 3 cases and from isoelectric or slightly inverted to decidedly inverted in the remaining 8. Transitory augmentation of acetylcholine probably affected the myocardium proper or caused coronary vasoconstriction which resulted in anoxemia that did not produce cardiac pain. Carotid sinus pressure produced slowing of the heart rate in 382 cases (80 per cent) and prolongation of auriculoventricular conduction in about one third of all the cases; the right and the left sides were about equally effective in prolonging the P-R interval. Cardiac inhibitory effects occurred with about equal frequency in control cases, i. e., without evidence of coronary artery disease, and in patients who did show evidence of impairment in coronary circulation, namely, cardiac pain and/or electrocardiographic signs of myocardial fibrosis related to coronary artery disease.

**Brown Induration of the Lungs.**—McLetchie and Colpitts report a case of idiopathic pulmonary hemosiderosis in a boy who died at the age of 4 years and 5 months, after periodic, acute and severe episodes of anoxemia accompanied with a pulmonary consolidation resulting from a massive and universal diapedesis of red blood cells from the pulmonary capillary vessels. Recovery from several acute attacks of dyspnea and cyanosis was possible with rest and oxygen by absorption of the alveolar hemorrhage. The fatal attack was similar to the previous attacks but with the addition of hemoptysis. Necropsy revealed an extreme degree of brown induration of the lungs and a complete lack of primary pathologic change outside the lungs. The periodic attacks of severe anoxic anoxemia gave rise to a characteristic clinical condition referable to symptoms and signs associated with massive lysis of the blood, defective pulmonary aeration, and right heart failure. The symptoms were present when the boy was 1 year old. They may be seen in children of several months to sixteen years of age. Between attacks there may be signs of deficient pulmonary aeration. The essential nature of the disease is unknown. Attention is drawn to two possible primary conditions: (1) inelasticity of the lungs due to hypoplasia of the elastica and (2) a vasomotor abnormality of the lesser circulation.

**Esophageal Varices.**—According to Ripstein there were 64 patients admitted to the Royal Victoria Hospital, Montreal, for bleeding esophageal varices in the past fifteen years. Of these, 23 died in the hospital. An incomplete follow-up reveals that most of the remainder were dead within five years. Two cases, 1 of Banti's syndrome with cirrhosis of the liver and esophageal varices in a man aged 40, and 1 with cirrhosis of the liver and esophageal varices in a man aged 59, are reported in which end-to-end splenorenal anastomosis was done. The operation did not improve hepatic function in the first case, but, as of the time of writing, the bleeding had not recurred. The varices decreased considerably in size. The esophageal varices in the second case regressed; the ascites had decreased considerably two months after the operation. Relief of portal hypertension may or may not cause the varices to disappear, but the bleeding tendency is relieved in most cases. Removal or obliteration of the varices would be much more rational as a secondary procedure after the portal pressure has been reduced to a normal level. It is advisable to wait several months before considering such an operation, because in many cases the varices slowly decrease in size and are eventually obliterated. The operation does not carry an unduly high mortality in patients with adequate hepatic function.

## Journal of Bacteriology, Baltimore

**57**:575-666 (June) 1949. **Partial Index**

Effect of Surface-Active Agents on Phagocytosis. L. J. Berry, R. W. Starr III and E. C. Haller.—p. 603.
Mineral Deficiencies in Complex Organic Media as Limiting Factors in Sporulation of Aerobic Bacilli. J. W. Foster and F. Heiligman. —p. 613.
Shigella Nomenclature. W. H. Ewing.—p. 633.
Biochemical Factors Influencing Sporulation in Strain of Bacillus Cereus. J. W. Foster and F. Heiligman.—p. 639.

## Journal of Clin. Endocrinology, Springfield, Ill.

**9**:481-578 (June) 1949

Preparation of Human Insulin for Experimental Use. W. Franklin and F. C. Lowell.—p. 481.
Sympathicotropic (Leydig) Cell Tumor of Ovary with Virilism: Report of Case. D. Waugh, E. H. Venning and D. McEachern.—p. 486.
Endocrine Finding Apparently Characteristic of Gout: Very Low Urinary 17-Ketosteroid Excretion with Clinically Normal Androgenic Function. W. Q. Wolfson, H. S. Guterman, R. Levine and others.—p. 497.
Pregnancy in Addison's Disease: Report of 4 Patients. A. I. Knowlton, G. H. Mudge and J. W. Jailer.—p. 514.
Hormonal Alterations in Men Exposed to Heat and Cold Stress. H. J. Stein, R. A. Bader, J. W. Eliot and D. E. Bass.—p. 529.
Changes in Urinary Uric Acid-Creatinine Ratio After Electrically Induced Convulsions in Man. M. D. Altschule, L. H. Altschule and K. J. Tillotson.—p. 548.
Loss of Axillary and Pubic Hair in Patient with Addison's Disease and Regular Menstruation: Case Report. J. C. Mussio Fournier, E. Pollack and J. J. Lussich Siri.—p. 555.
Metabolism of Estrogens: Review. J. W. Jailer.—p. 557.

## Journal of Immunology, Baltimore

**62**:257-352 (July) 1949

Assay of Antigenic Polysaccharides and Vaccines. K. A. Ludwig, F. J. Murray and E. J. Staubach.—p. 257.
Serologic Diagnosis of Mumps. Comparative Study of Three Methods. J. K. Aikawa and G. Meiklejohn.—p. 261.
Serologic Reactivity of Mucoid Strains of Escherichia Coli. S. D. Henriksen.—p. 271.
*Studies on Diphtheria: IV. Skin Factor in Schick Reaction. B. Vahlquist and C. Högstedt.—p. 277.
Comparison of Diagnostic Methods for Western Equine and St. Louis Encephalitis. G. Meiklejohn, E. Rust and O. Brunetti.—p. 293.
*Level of Serum Antibody Associated with Intracerebral Immunity in Monkeys Vaccinated with Lansing Poliomyelitis Virus. I. M. Morgan. —p. 301.
Bovine Plasma Albumin in Buffered Saline Solution as Diluent for Viruses. G. W. A. Dick and R. M. Taylor.—p. 311.
Influence of Certain Serum Factors on Neutralization of Western Equine Encephalomyelitis Virus. T. F. Dozois, J. C. Wagner, C. M. Chemerda and V. M. Andrew.—p. 319.
Hemagglutinating Substances for Human Cells in Various Plants. W. C. Boyd and R. M. Reguera.—p. 333.
Neutralization Technique in Tsutsugamushi Disease (Scrub Typhus) and Antigenic Differentiation of Rickettsial Strains. J. P. Fox.—p. 341.

**Skin Factor in Schick Reaction.**—Vahlquist and Högstedt point out that Jensen in 1931 was probably the first to stress that the correlation between the degree of the Schick reaction and the antitoxin titer varies in different subjects. It is, therefore, not correct to use the term "standard Schick threshold." Some Schick-negative children in Jensen's study had antitoxin titers as low as 0.0005 antigen unit per cubic centimeter. Subsequent investigators have confirmed these results, but they objected to Jensen's conclusion that the value of the negative Schick reaction is restricted. They argued that subjects with negative Schick reaction may have a good potential immunity even when the amount of circulating antitoxin is low. The authors performed Schick tests and antitoxin titrations on 143 subjects, including persons with no demonstrable diphtheria antitoxin in their blood, persons with diphtheria antitoxin in their blood due to active immunization and subjects with diphtheria antitoxin in their blood due to passive immunization with homologous antidiphtheric serum. They conclude that the comparatively wide individual variations in the ratio between the size of the Schick reaction and the antitoxin titer of the blood are only partially explained by potential immunity. Nonspecific individual differences of the skin play a role, which should not be neglected for the specific tissue factors.

**Immunity in Monkeys Vaccinated with Lansing Poliomyelitis Virus.**—According to Morgan a high degree of immunity can be induced in monkeys by intramuscular vaccination with poliomyelitis virus. This means of immunization

has served as a means of differentiating immunologic types of poliomyelitis. In addition, it provides a basis for the quantitative study of antibody level in relation to immunity, which is the subject of the present study. Rhesus monkeys were inoculated intramuscularly with graded amounts of active Lansing poliomyelitis virus. The proportion of monkeys immune to the subsequent intracerebral injection of active virus was found to rise with increasing dosage of vaccine. In 79 vaccinated monkeys, serum taken before intracerebral challenge was titrated by mouse neutralization test. As the serum titer rose, a greater proportion proved to be immune. The minimal level of serum antibody associated with complete immunity of the group was found to be 3.0 (1/1,000 dilution of serum). These quantitative data give further information on the required level of serum antibody associated with immunity in an experimental animal. They also provide an effective means of vaccination of monkeys which has served as a basis for type differentiation of strains of poliomyelitis virus.

## Journal of Infectious Diseases, Chicago

**85**:1-106 (July-Aug.) 1949

Exponential Development of Penicillin Resistance by Neisseria. F. Mills.—p. 1.
Physiological and Pathological Observations on Four Strains of Trypanosoma Cruzi. R. Von Brand, E. J. Tobie, R. E. Kissling and G. Adams.—p. 5.
*Diphtheria Antitoxin Estimations in Blood of Adult Population of Bergen, Norway, Just After Diphtheria Epidemic. T. M. Vogelsang.—p. 17.
Streptomycin Studies in Tularemia. S. S. Chapman, C. M. Downs, L. L. Coriell and S. F. Kowal.—p. 25.
Concentration of Mumps Virus. G. F. Forster and E. Carson.—p. 62.
Release of A2 Isoagglutinogen-like Substance of Infectious Organisms into Human Blood Serum. J. Oliver-González and L. M. González.—p. 66.
*Nocardiosis, with Report of 3 Cases of Actinomycosis Due to Nocardia Asteroides. F. C. Tucker and E. F. Hirsch.—p. 72.
Enteric Organisms from American Cockroach. R. S. Bitter and O. B. Williams.—p. 87.
Induced Resistance to Bacitracin in Cultures of Staphylococcus Aureus. J. L. Stone.—p. 91.
Behavior of Pasteurella Pestis in Glycerin and Rhamnose Mediums. T. H. Chen.—p. 97.
Mucolytic Enzyme Systems: VI. Inhibition of Hyaluronidase by Serum in Infectious Diseases. M. L. Grais and D. Glick.—p. 101.

**Diphtheria Antitoxin in Blood.**—Vogelsang states that there was a slow decline of diphtheria in Bergen, Norway between World War I and World War II. In 1919 the rate was 8.73 per thousand inhabitants. This figure had declined to 1.45 in 1935, with the lowest level (0.02) in 1940. The diptheria mortality was 0.46 per thousand inhabitants in 1919 and had decreased to 0.09 in 1931. In the period from 1935 through 1940 there was not a single death from diphtheria in Bergen. In Germany during the years preceding World War II, there were extensive epidemics of diphtheria and it was feared that an epidemic would break out in Bergen after it was occupied by the Germans in April 1940. The incidence of diphtheria did not rise until the end of 1941, but during the following years, it assumed epidemic proportions. Whereas in the years before the epidemic the mitis type of diphtheria organism had predominated and the type intermedius had become dominant at the beginning of the epidemic, type gravis gradually became dominant as the epidemic continued. In 1942 compulsory diphtheria immunization was carried out on the school children in Bergen and has been continued. It was extended to other age groups when, during the epidemic, there was a shift in the age distribution of diphtheria to higher age groups. In 1942, 13 per cent of the patients were over the age of 30; this figure increased to 35 per cent by 1947. Determination of the antitoxin titer of 1,000 persons after the epidemic revealed that the antitoxin spectrum of the adult population of Bergen was low. Fifty-nine per cent of 716 unvaccinated persons had an antitoxin content of 0.01 per cubic centimeter or less. Fifty-three per cent of these persons had passed the age of 30. Eighty-eight unvaccinated persons who had previously had diphtheria had similarly low antitoxin titers. Of 196 persons vaccinated with diphtheria toxoid, 93 per cent had an antitoxin titer of more than 0.01 unit per cubic centimeter. The extensive vaccination which has been carried out against diphtheria of late years in Bergen, notably among school children and young persons, seems to have had an influence on the antitoxin spectrum.

**Nocardiosis.**—Thirty-seven cases of infection with Nocardia asteroides were culled from the literature. The mortality rate appears high: only 5 of the 37 patients could be considered as having recovered, and all 5 patients received sulfonamide therapy in addition to other forms of treatment. The infection was pulmonary in 33 cases. Metastatic abscesses of the brain were present in at least 11. Three cases of nocardiosis due to N. asteroides, 2 of them terminating fatally, are decribed by the authors. The organisms isolated from the lesions belong to the relatively rare aerobic, variably acid-fast group of Actinomyces. The acid fastness of N. asteroides is a variable property. In distinguishing this group of organisms from other pathogenic actinomycetes, much more emphasis should be given to other properties, such as the readiness with which they may be cultivated on artificial mediums, their cultural characteristics, their virulence for laboratory animals and the usual absence of "sulfur granules" and "club formation" at the periphery of the mycelial masses. The importance of the actinomycotic infections lies in the possibility of their being confused with tuberculosis. Nocardiosis should be considered in all patients with obscure or unusual chronic infections, especially when repeated attempts to demonstrate tubercle bacilli have failed. Treatment with sulfadiazine or other sulfonamides drugs appears to be preferable to the use of antibiotics such as penicillin and streptomycin in the aerobic type of actinomycotic infection.

## Journal of Investigative Dermatology, Baltimore

**13**:1-46 (July) 1949

Phytopharmacologic Studies on Blood of Psoriasis. D. I. Macht.—p. 1.
Aureomycin Therapy of Disseminated Cutaneous Herpes Simplex (Kaposi's Varicelliform Eruption). R. L. Baer and O. B. Miller.—p. 5.
*Therapeutic Value of Aureomycin in Dermatitis Herpetiformis. H. M. Robinson, H. M. Robinson Jr. and R. C. V. Robinson.—p. 9.
Treatment of Case of Kaposi's Varicelliform Eruption with Aureomycin. E. S. Bereston and P. E. Carliner.—p. 13.
Various Kinds of Eczematoid Eruptions Attributable to Exposure to Foods. A. F. Coca.—p. 17.
Reactions to Local Use of Thephorin. F. A. Ellis and W. R. Bundick.—p. 25.
Experimental Determination in Human Subjects of Duration of "Antihistaminic" Activity of Orally Administered Compounds. D. J. Perry and D. L. Hearin.—p. 29.
*Use of N-Ethyl-O-Crotono-Toluidide in Treatment of Scabies and Various Pruritic Dermatoses. M. Couperus.—p. 35.
Apparent Association of Lichen Planus with Vascular Hypertension. F. W. Lynch and H. E. Michelson.—p. 43.

**Aureomycin in Dermatitis Herpetiformis.**—Robinson and co-workers treated 5 patients with dermatitis herpetiformis with aureomycin by mouth. The dosage schedule was 250 mg. four times daily for two days and thereafter 500 mg. four times daily for the duration of treatment, which was continued for four weeks. Relief from itching and involution of vesicles occurred in one to two weeks. Pronounced subjective and objective improvement was noted at the end of one week's treatment, when a total of 12 Gm. had been administered. In 4 of the 5 patients there were slight recurrences after use of the antibiotic was discontinued. Nausea was encountered in 3 patients, but all were anxious to resume the aureomycin therapy when there were recurrences. Diarrhea was severe in 1 patient; this patient refused to continue use of the drug. The authors believe that the reactions may be avoided if the dose of the drug is kept at 1 Gm. daily. The patients stated that this method of treatment was superior to all other forms of treatment they had received previously.

**N-Ethyl-O-Crotono-Toluidide in Scabies and Pruritic Dermatoses.**—Couperus treated 70 patients with scabies with a 10 per cent concentration of N-ethyl-o-crotono-toluidide in a washable ointment base. The patients were asked to apply the ointment to the entire body except the head on two successive nights. It was suggested that on the third night, after completion of treatment, the patient take an ordinary soap and water bath. All the patients were cured. Three patients required more than the two routine applications before all clinical evi-

dence of disease disappeared. There were no local or systemic reactions. A second series, 124 patients, was treated with the same preparations for the relief of pruritus in a variety of dermatoses. Most of the cases were of neurodermatitis, pruritus ani et vulvae and dermatitis venenata. Eighty-two patients obtained complete relief, lasting usually six to eight hours; 34 found considerable relief, and 8 found little or no relief. There was no evidence of any systemic reaction to the drug, and there were 3 patients with a local reaction, mild erythema which proved to be due to the washable ointment base.

## Journal National Malaria Society, Columbia, S. C.

**8**:115-174 (June) 1949. **Partial Index**

Malaria Control Progress and Problems. F. Tetzlaff.—p. 115.
Ascorbic Acid Content of Adrenal Glands of Chicks Infected with Plasmodium Gallinaceum. E. S. Josephson, D. J. Taylor, J. Greenberg and E. M. Nadel.—p. 132.
Laboratory Studies on Resistance of Anopheles Quadrimaculatus to DDT and Other Insecticides. R. W. Fay, W. C. Baker and M. M. Grainger. —p. 137.
Anopheles Quadrimaculatus Activity Patterns in Laboratory on Untreated and DDT-Treated Surfaces. R. W. Fay and E. H. Sheppard.—p. 147.
Overwintering of Anopheles Crucians Wied. in South Carolina. W. C. Frohne and J. W. Hart.—p. 171.

## Journal of Neurophysiology, Springfield, Ill.

**12**:225-288 (July) 1949. **Partial Index**

Effect of Curare on Cortical Responses Evoked by Afferent Stimulation. M. Ostow and F. Garcia.—p. 225.
Unipolar Electromyograms of Normal and Denervated Human Muscle. H. Jasper and G. Ballem.—p. 231.
Action Potentials of Cerebellar Cortex in Response to Local Electrical Stimulation. R. S. Dow.—p. 245.
Selective Destruction of Large Motoneurons by Poliomyelitis Virus. I. Conduction Velocity of Motor Nerve Fibers of Chronic Poliomyelitis Patients. R. Hodes.—p. 257.

## Journal of Neurosurgery, Springfield, Ill.

**6**:269-350 (July) 1949

Caries Cranii (Tuberculosis of Flat Bones of Vault of Skull). A. C. de Vet.—p. 269.
Description of Skin Galvanometer That Gives Graphic Record of Activity in the Sympathetic Nervous System. C. P. Richter and F. G. Whelan.—p. 279.
*Cerebral Hemispherectomy: Report of Case Ten Years After Operation. E. Bell Jr. and L. J. Karnosh.—p. 285.
*Traumatic Subdural Hematoma—Aucte, Subacute and Chronic: Analysis of Seventy Operated Cases. F. Echlin.—p. 294.
Use of Dry Oxidized Cellulose as Primary Hemostatic Agent in Neurosurgery. J. E. Scarff, B. Stookey and F. Garcia.—p. 304.
Classification of Craniostenosis. D. Fairman and G. Horrax.—p. 307.
Arnold-Chiari Deformity Without Bony Anomalies. H. S. Swanson and E. F. Fincher.—p. 314.
Note on Identification of Motor Supply to the Detrusor During Anterior Dorsolumbar Rhizotomy. R. A. Kuhn.—p. 320.
*Duplication of the Spinal Cord (Diplomyelia): Account of Clinical Example with Consideration of Other Reports. W. Pickles.—p. 324.

**Cerebral Hemispherectomy.**—Bell and Karnosh believe that cerebral hemispherectomy should not be considered except in gliomas that are located well away from the midline and that have not invaded too deeply into the basal ganglions. The indications narrow down to the occasional slowly growing oligodendroglioma and astrocytoma involving the middle portion of the hemisphere. In all 4 of their patients the relative freedom from severe physical handicap and gross mental defect after removal of almost half the cerebrum was striking. They describe a patient in whom most of the right cerebral hemisphere was removed in March 1938. Coronal sections of the removed hemisphere show that the astrocytoma occupies the white matter in the third frontal convolution anteriorly and extends upward and posteriorly into the white matter of the parietal lobe. The line of surgical section shows that the caudate nucleus, the putamen and even the outer portion of the globus pallidus have been sacrificed. The chief structures remaining in situ on the right side of the brain were the hypothalamus, the thalamus and about four-fifths of the globus pallidus. Mesial portions of the hippocampal and fusiform gyri were spared also. The patient returned home and undertook his old job of operating a small restaurant with the assistance of his wife. A conference with the wife gave the authors a picture of the mental status of the patient ten years after operation. He still worries little about finances. He had never shown asocial or antisocial tendencies. He takes home life seriously and occupies himself about the house and yard. He continues to be neat, clean and sociable and to recount numerous stories. His disposition is generally good. He becomes emotionally upset easily, but these moods pass quickly. He is still a good poker and pinochle player. He does not show a decreased tolerance to alcohol. His health has been excellent. The authors conclude that the sensory and motor postoperative changes after cerebral hemispherectomy are not incapacitating if the paleostriatum and thalamus remain essentially intact.

**Traumatic Subdural Hematoma.**—Echlin points out that in the past it has been common practice to class all subdural hematomas as acute or chronic. In reviewing 70 cases of subdural hematomas that have been operated on over a twenty month period (1941-1942) at Bellevue Psychiatric Hospital, the author stresses that there are also more or less subacute conditions. In order to emphasize the difference in the clinical course of the illness, and in the pathologic nature of the hematomas in the variout patients, he analyzes them in groups according to the time elapsed since injury. Many of the patients in the subacute group, although they remain drowsy or confused in some instances, have had time to recover, or largely recover, from their initial brain injury, but lapse into deepening drowsiness or show other signs of a severe progressive intracranial lesion in a week or several weeks after trauma. At operation, the hematomas in these persons vary in structure and, pathologically, at times more closely resemble the chonic than the acute type of lesion. Many patients suffering from large collections of blood in the subdural space present neither an acute nor a chronic picture clinically or pathologically. Unless this is stressed, the uninitiated may fail to be on the alert for the subdural hematoma that ends in death in one week to several weeks after injury.

**Duplication of the Spinal Cord.**—Pickles reports on a girl who at the age of 10 began to limp and in whom examination showed a small, short right foot with high arch and persistent inversion, with atrophy and general weakness of the muscles of the entire right leg; there was anesthesia to light touch on all the toes on the right, with hypesthesia to touch and pinprick up to the knee. Roentgenograms of the spine showed flattening and deformity of the tenth, eleventh and twelfth dorsal bodies, with narrowing of the interspaces, partial absence of the eleventh and twelfth dorsal neural arches and complete absence of the first lumbar arch. Pantopaque® (ethyl iodophenylundecylate) myelography revealed a split in the oil column at the level of the congenital defect, with a large irregular defect at the tenth dorsal body. An exploration to rule out the presence of a tumor revealed a ventral bony projection, which was found to pierce the membranes and the cord and to be firmly attached to the underlying vertebral body. The dura was opened above the bony spur; this exposed an apparently normal cord which divided to pass around the bony partition. Opening of the dura below the obstruction showed that the split in the cord continued, with obvious separation of the two parts, for at least 2 inches (5 cm.). The divided cord was enclosed around the bony partition in two separate tubes of dura and arachnoid. Below the obstruction the divided cord had a single dural and arachnoid covering with separate pial envelopes. It was possible to remove the bony partition. The dura was closed with interrupted silk stitches, and the wound was closed in the usual manner. The patient was discharged on the twenty-fifth postoperative day. At this time her pain had disappeared, she could move her toes and foot better, and her anesthesia had lessened. The published reports covering 46 cases reveal that in most of the cases the condition was found at autopsy and that in many instances it was not suspected during life. In 6 instances the condition was found at operation; 5 of these patients survived. Some observers felt that only pseudoduplication ever occurs. The contention is erroneous, in view of reports showing two practically complete cords, each with its full complement of nerve roots. The most reasonable explanation of the condition seems to be that it represents an incipient form of twinning.

## Journal of Nutrition, Philadelphia

**38**:275-404 (July) 1949. **Partial Index**

Value of Rutin and Quercetin in Scurvy. A. M. Ambrose and F. De Eds.—p. 305.
Effect of Retention of Nitrogen in Casein or Lactalbumin Hydrolysates on Regeneration of Plasma Proteins of Protein-Depleted Dogs. B. F. Chow, C. Alper and S. De Biase.—p. 319.
Enhancement of Nutritive Value of Wheat Gluten by Supplementation with Lysine, as Determined from Nitrogen Balance Indices in Human Subjects. W. S. Hoffman and G. C. McNeil.—p. 331.
Influence of Thyroid on Utilization of Vitamin A. C. B. Heimer, H. L. Maslow and A. E. Sobel.—p. 345.
Vitamin Studies in Middle-Aged and Old Individuals: III. Thiamine and Pyruvic Acid Blood Concentrations. E. Kirk and M. Chieffi. —p. 353.
Studies on Comparative Nutritive Value of Fats. H. J. Deuel Jr., S. M. Greenberg, E. E. Straub and others.—p. 361.
*Nutritive Properties of Protein in Different Cuts of Beef. R. Hoagland, O. G. Hankins, N. R. Ellis and G. G. Snider.—p. 381.

**Nutritive Properties in Different Cuts of Beef.**—Hoagland and his associates feel that, in view of the high price of beef, there is need for information concerning the nutritive properties of the meat of one cut as compared with those of another. They investigated the growth-promoting values of the protein in six different cuts of beef from each of two carcasses, one of a Shorthorn steer graded "high good" and the other a Hereford cow graded "commercial," by feeding tests with young male albino rats. The cuts tested were: round, loin, rib, chuck, neck and combined fore and hind shanks. When protein constituted 7.5 per cent of the diets, there were no significant differences in the nutritive values of the protein in the different cuts from the Shorthorn steer. In tests with the cuts from the Hereford cow, the protein in the round had a higher value than that in the other cuts except the shanks. When protein constituted 10 per cent of the diets, there were no significant differences in the nutritive values of the protein in the different cuts of beef, either from the Shorthorn steer or from the Hereford cow. When the diets contained 12.5 per cent protein, the growth-promoting values of the protein in the rib and neck from the Shorthorn steer were slightly lower than the values for the shank, round or chuck. The protein in the rib from the Hereford cow had a slightly lower value than the protein in the chuck. The average growth-promoting value of the protein at each level of intake was slightly higher for all the cuts from the Shorthorn steer than for those from the Hereford cow. The average nutritive value of the protein in the cuts of beef from the Shorthorn steer, at the 7.5 per cent level of protein intake, was approximately the same as the value for dried skim milk. When the diets contained 10.0 or 12.5 per cent protein, the beef protein was of higher nutritive value than the milk protein.

## Journal of Pediatrics, St. Louis

**35**:135-274 (Aug.) 1949

*Oral Penicillin for Children with Rheumatic Fever. J. W. Hofer. —p. 135.
Further Studies on Oral Penicillin in Prophylaxis of Recurrent Rheumatic Fever. M. M. Maliner, S. D. Amsterdam and C. C. Arreche.—p. 145.
*Pancreatic Achylia and Glycosuria Due to Cystic Disease of the Pancreas in a 9-Year-Old Child. H. Anfanger, M. H. Bass, R. Heavenrich and J. J. Bookmar —p. 151.
Grid Prodrome Phenomenon in Celiac Disease: Report of Four Cases. A. B. Coleman.—p. 165.
Stricture of the Urethra in Children. M. F. Campbell.—p. 169.
Congenital Anal Stricture. J. Liburt.—p. 180.
Tuberculin Patch Test: Further Study of Modifications of Normal Procedure. J. Schwartzman and M. Cerone.—p. 185.
Leprosy, a Disease of Childhood with Special Reference to Early Findings in Eye, Ear, Nose and Throat of Children Examined at the National Leprosarium at Carville, La. D. C. Elliott.—p. 189.
Potassium Bromate Poisoning. W. Kitto and K. W. Dumars.—p. 197.
Feeding Premature Infants: Comparison of Four Groups of Premature Infants Fed Different Milk Mixtures. J. W. Bruce, L. J. Hackett Jr. and J. E. Bickel.—p. 201.
Pyloric Stenosis in One of Identical Twins. R. F. Garrison.—p. 207.
Tetany in Newborn Twins Coincident with Maternal Toxemia. H. Lubenstein.—p. 210.
Pseudopeptic Ulcer Syndromes in Children. S. R. Warson, S. Turkel and H. S. Schiele Jr.—p. 215.
Congenital Indifference to Pain. D. I. Arbuse, M. B. Cantor and P. A. Barenberg.—p. 221.
Experiment in Sex Education at a Boys' Summer Camp. L. M. Shapiro. —p. 227.

**Oral Penicillin in Rheumatic Fever.**—Hofer administered penicillin by mouth in the fasting state to 63 children between the ages of 4 and 13 years, who were chronically ill with varying degrees of active rheumatic fever or active rheumatic carditis. Each child received 200,000 units of the drug daily in equally divided doses of 100,000 units given one-half hour before breakfast and 100,000 units given one-half hour before supper. The penicillin tablets were buffered with calcium carbonate and flavored and sweetened to improve their palatability. No confirmed group A hemolytic streptococcic infection of the upper part of the respiratory tract appeared in the 63 children receiving penicillin by mouth over a seven month period; 1 child was a confirmed carrier. Sixty-four children receiving placebos served as controls during this period. Four had confirmed group A hemolytic streptococcic infections of the upper part of the respiratory tract, and 11 were proved carriers. Two successive blood plasma bioassays for penicillin, each conducted on the same plasma specimen of 6 older children of varying age and weight, demonstrated that a single dose of 100,000 units of buffered penicillin in a fasting state produces a satisfactory therapeutic blood plasma penicillin level for approximately three hours following each administration. Employing two technics for the estimation of penicillin resistance in fifty-seven strains of group A hemolytic streptococci recovered in throat cultures of the placebo-treated children, there was no demonstrable increase in resistance among the strains during this brief study. Eight thousand and five hundred doses of penicillin were administered by mouth during the seven month study. No untoward reactions of penicillin sensitivity were observed. Routine laboratory examinations of blood and urine to detect and correct any potential toxic manifestations arising from its use were unnecessary with orally administered penicillin as distinguished from the potential hazard associated with administration of the sulfonamide compounds. Orally administered penicillin offers considerable promise in protecting chronically ill rheumatic children from group A hemolytic streptococcic infections of the upper part of the respiratory tract.

**Pancreatic Achylia and Glycosuria.**—Anfanger and co-workers report 1 case of pancreatic achylia associated with glycosuria due to multiple cysts of the pancreas in a boy aged 9 years, whose mother had mild diabetes during her pregnancy before the birth of the patient. This may have had some bearing on the boy's pancreatic anomalies. Intestinal obstruction developed, and at operation an abdominal mass was found, which on two separate biopsies proved to be pancreas studded with multiple small cysts. Microscopic examination revealed a different lesion from that seen in congenital cystic fibrosis of the pancreas but closely resembling that found in polycystic disease as described by Lindau. Extreme emaciation and evidence of vitamin A deficiency were present. These were accompanied with pancreatic achylia, failure to absorb vitamin A, a flat gelatine tolerance reaction and glycosuria. After one year, the patient's general condition was good, although his height and weight were retarded and infections of the upper part of the respiratory tract developed frequently with rapid loss of weight. His mild glycosuria persisted.

## Kansas Medical Society Journal, Topeka

**50**:373-424 (Aug.) 1949

Office Gynecology. R. J. Crossen.—p. 373.
Strictures of Bile Ducts. T. G. Orr Jr.—p. 379.
Amebiasis: Experiences at Veterans Hospital. R. Chess and N. Uhr. —p. 383.
*Tularemia: Report of Case of Primary Tularemic Tonsillitis in Which Bacterium Tularense was Isolated from Sputum. R. A. Jordan and C. M. Downs.—p. 390.

**50**:1-A-76-A (Aug.) 1949. **Partial Index**

Cancer of Stomach. W. L. Palmer.—p. 8-A.
Cancer of Lung. L. V. Ackerman.—p. 13-A.
Tumors of Ovary. H. E. Schmitz.—p. 18-A.
Prospects in Cancer Control. C. S. Cameron.—p. 34-A.
Diagnosis of Leukemias and Malignant Lymphomas. T. Cooper.—p. 41-A.
Diagnosis and Treatment of Endometrial Cancer. H. E. Schmitz. —p. 47-A.
Diagnosis and Treatment of Cancer of Cervix. W. W. Wasson.—p. 51-A.
Malignant Melanoma of Skin. L. V. Ackerman.—p. 60-A.

**Tularemic Tonsillitis.**—Jordan and Downs report a man, aged 23, who was hospitalized on Nov. 18, 1947, because of fever, headache, malaise and sore throat of two days' duration. He was employed as a technician in the tularemia research laboratory. On Nov. 14, 1947, while he was transferring some liquid cultures of Bacterium tularense, a cotton plug which had

been placed in the bore of the transferring pipette became dislodged and he aspirated some of the culture. He rinsed his mouth immediately with 70 per cent alcohol. His first symptoms were noted two days later. Specimens of the patient's blood were inoculated into guinea pigs on November 20, but the pigs did not die. On the same day throat washings were obtained from the patient and inoculated by the intraperitoneal route into each of two guinea pigs. Both pigs died three days later; at autopsy there were findings typical of tularemia. Subsequent culture of the guinea pig organs yielded Bact. tularense. A presumptive diagnosis of tularemia was made on November 20, and treatment with streptomycin was begun. The patient responded well and was discharged from the hospital afebrile and free of symptoms November 25. The patient returned as an outpatient December 1, complaining of malaise and soreness in the left side of his throat. Examination of the pharynx revealed an ulcerated area over the left tonsil. Local treatment of the ulcer with silver nitrate resulted in no improvement. Treatment with streptomycin was again started in a dosage of 100,000 units intramuscularly every three hours for a total of 3,700,000 units. The tonsillar ulcer healed rapidly with streptomycin therapy. On December 10, twenty-five days from the onset of his symptoms, the patient felt well and was discharged from the hospital as cured.

## Kentucky Medical Journal, Bowling Green

**47**:247-288 (July) 1949

Problem of Vagotomy in Treatment of Peptic Ulcer. W. Walters, B. C. Brownson and S. K. Phillips.—p. 254.
Medical Treatment of Cerebrovascular Accidents. F. K. Sewell.—p. 265.
Leukorrhea, Diagnosis and Treatment. J. Siehl.—p. 270.
Dysmenorrhea: Recent Trends in Treatment with Report of 42 Cases. L. H. Liebert.—p. 273.
Medical Uses of Vitamin E. H. B. Mack.—p. 276.

**47**:289-337 (Aug.) 1949

Liver Biopsy in Diagnosis of Hepatic Disease. C. W. Kumpe.—p. 300.
Hypertensive Heart Disease. A. L. Cooper.—p. 305.
Indications for Hysterectomy. L. A. Gray.—p. 313.
Problems of Neonatal Period. W. T. Temple.—p. 318.
*Problem of Rabies Prevention. D. N. Pickar.—p. 320.
Newer Antibiotics. F. Coleman.—p. 326.

**Prevention of Rabies.**—Pickar discusses the management of a person bitten by a dog. He reviews the indications for vaccine therapy, its complications together with their prevention and treatment. Vaccine should be given only to persons who have had a definite exposure. Those receiving vaccine should be observed carefully for signs of sensitivity to the vaccine, and the sensitive person should be desensitized according to a recommended schedule. Persons with neuroparalytic or other reactions to the vaccine should be treated with antihistaminic agents.

## Laryngoscope, St. Louis

**59**:829-928 (Aug.) 1949. **Partial Index**

*Carotid Pain. J. A. Hilger.—p. 829.
Cancer of the Nose: Treatment and Plastic Repair. J. B. Erich.—p. 839.
Reconstruction of Nasal Septum. D. M. Lierle and W. C. Huffman.—p. 858.
Use of Magnet in Tracheobronchial Tree, Esophagus, Stomach and Duodenum. M. Equen, G. Roach and R. Brown.—p. 873.
Stapedioparalytic Phonophobia ("Hyperacusis") in a Deaf Ear. Case Reports Including Studies on Analysis of Phenomenon and Suggestions for Possible Applications of the Phonophobia Test. K. Tschiassny.—p. 886.

**Carotid Pain.**—Hilger states that irregularity in autonomic balance produces clinical pictures ranging from Raynaud's disease to neurovascular arthropathies and from peptic ulcer to ulcerative colitis. Clinical manifestation of autonomic imbalance is perhaps most common in the cranial segments of the sympathetic and parasympathetic systems. It is exhibited principally in alterations in the vasomotor control of the carotid arterial tree. Innervation seems to be more profuse at the arteriolar than the arterial level. Angiospasm in vessels of arteriolar caliber is mediated through sympathetic innervation. The ischemic capillary becomes dilated, and transudation results. There is evidence that this vascular change is the basis of the wheal formation and edema of the allergic reaction. A common site of dilatation is at the carotid bifurcation. The patient usually complains of the recurrent and abrupt onset of unilateral sore throat with the appearance of a "gland" in the neck. The bifurcation is palpable as a firm, extremely tender mass at the hyoid level, and it pulsates. So-called facial neuralgic pain usually is angiodilating pain. Removal of the sphenopalatine ganglion has little to recommend it in the relief of cranial vascular pain because the sympathetic innervation of the carotid branches does not centralize well at the sphenopalatine. The surgical trauma of intranasal septal surgery gives temporary relief to angiodilating pain because trauma alters autonomic balance for a time. The same may be said for removal of the edematous and hyperplastic mucosa of the paranasal sinuses. Edema follows severe arteriolar angiospasm and results in swelling. In the internal maxillary arterial distribution this results in edema and hypersecretion of the mucosa of the nasal and paranasal sinuses; in the periorbital vessels it results in conjunctival injection; in the superior thyroid artery it can produce severe intracapsular swelling; in the external maxillary, edema of the lip develops; in the transverse facial, edema of the lower lid may be recurrent; in the ascending pharyngeal, pharyngeal edema and severe sore throat simulate pharyngitis; in inferior dental and alveolar branches the dull, pulsating throb of apical abscess is simulated by edema of the pulp and the like. The author gives several illustrative case histories. Medicines are of little use. With psychiatric care, use of the dilating properties of nicotinic acid, occasional barbiturate sedation and peripheral neural block with tripelennamine hydrochloride, the frequency of angiodilating pain and vasomotor labyrinthine attacks can be diminished.

## Medical Annals of District of Columbia, Washington

**18**:335-388 (July) 1949

Aureomycin in Various Infections: Report of 180 Cases and Review of Clinical Literature. H. F. Dowling, M. H. Lepper, E. R. Caldwell Jr. and others.—p. 335.
Operative Treatment of Ureteral Strictures. J. C. Kimbrough.—p. 345.
Conservatism in Pelvic Surgery. R. W. Mohler.—p. 348.
Psychiatric Aspects of Asthma. G. N. Raines.—p. 354.

**18**: 389-440 (Aug.) 1949

Breast Care in Pregnancy. J. Parks.—p. 389.
Upper Extremity Pain: The Orthopedist's Point of View. I. W. Nachlas.—p. 394.
Coexistence of Diabetes Insipidus and Diabetes Mellitus. D. E. DeLawter.—p. 398.
Giant-Cell Tumor of the Thyroid Gland. D. Feriozi.—p. 401.
Patrick Manson and the Exotic Diseases. E. Podolsky.—p. 403.

## Michigan State Medical Society Journal, Lansing

**48**:793-952 (July) 1949

Public Health and Private Medical Practice: Unbeatable Team. H. Emerson.—p. 825.
Hysterectomy: Present-Day Indications. R. W. TeLinde.—p. 829.
Amebiasis and Its Complications: Diagnosis and Treatment. H. J. Kullman.—p. 832.
Management of Cerebral Palsy. F. B. House.—p. 843.
Correlation of Roentgenograms of Clubfeet with Basic Pathologic Anatomy. F. B. Kimball.—p. 848.
Thyrotropic Exophthalmos from Viewpoint of Ophthalmologist. F. H. Adler, H. G. Scheie and R. Dennis.—p. 852.
Intra-Uterine Volvulus of Ileum with Absorption of Ileum in Full-Term Pregnancy. F. E. Ludwig and C. A. Ludwig.—p. 858.
Nonsurgical Biliary Drainage for Acute Pancreatitis: 2 Case Reports. M. O. Cantor and W. W. Babcock.—p. 860.
Regional Enteritis. L. S. Fallis.—p. 864.
Urinary Amino Acid Wastage Studies Following Single Infusions of Amino Acid Mixtures: Preliminary Report. J. E. Harroun, S. Levey and C. J. Smyth.—p. 868.
Anesthetic Deaths in Infants and Children. M. D. Leigh and M. K. Belton.—p. 871.

## Military Surgeon, Washington, D. C.

**105**:103-190 (Aug.) 1949. **Partial Index**

Navy Medicine Beyond the Seas and on Safari. H. L. Pugh.—p. 103.
Army Medicine Around the World. E. E. Hume.—p. 110.
Diffuse Interstitial Fibrosis of Lungs. A. Golden and I. F. Tulis Jr.—p. 130.
Benign Retention Jaundice: Mechanism of Intermittent Jaundice in "Constitutional Hepatic Dysfunction": Report of Case. W. H. Corsby.—p. 139.
Skin Grafted Ileostomies. W. S. McCune and A. N. Bracher.—p. 144.
Improvised Well-Leg Traction: Description of Apparatus and Its Application to Military Surgery. J. W. Baluss Jr.—p. 146.
Neuropsychiatric Reconditioning Program in Peacetime Army. F. J. Ryan.—p. 149.
Atomic Radiation Effects: Release and Neutralization of Humoral Toxic Agents. R. deR. Barondes and D. I. Levine.—p. 153.

## New England Journal of Medicine, Boston

**241**:137-184 (July 28) 1949

Fractures of Tibial Spines. C. H. Bradford, R. W. Adams and H. K. Magill.—p. 137.
Otologic Aspects of Vertigo. J. J. Fischer.—p. 142.
Neurologic Aspects of Vertigo. D. E. Denny-Brown.—p. 144.
Vertigo as it Confronts the Internist. M. Aisner.—p. 145.
Thrombocytopenic Purpura Associated with Tuberculous Splenomegaly and Tuberculosis of Bone Marrow. B. A. Gouley, N. Blumberg and R. J. Grayson.—p. 147.
Strangulated Diaphragmatic Hernia Complicating Pregnancy: Report of Case. G. A. Bourgeois and W. T. Hood.—p. 150.
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Papillary Carcinoma of Renal Pelvis, with Extension into Ureter and with Metastases to Ureteral Mucosa.—p. 173.
Viral Hepatitis, Fulminant, Homologous Serum Type.—p. 176.

**241**:185-220 (Aug. 4) 1949

*Aureomycin Therapy in Pulmonary Involvement of Pancreatic Fibrosis (Mucoviscidosis). H. Shwachman, A. C. Crocker, G. E. Foley and P. R. Patterson.—p. 185.
*Posterior Tuberculous Sinuses of Vertebral Origin: Wound Revision and Closure with Streptomycin Permitting Early Spinal Fusion. J. J. Cincotti, A. M. Salzberg, E. W. Boone and J. B. Kelley.—p. 193.
Progressive Primary Tuberculosis in the Adult and Its Differentiation from Lymphomas and Mycotic Infections. D. T. Smith.—p. 198.
Hospital Administration as Medical Specialty. T. S. Hamilton.—p. 202.
Medical Progress: Viral Infections Contracted in the Laboratory. S. E. Sulkin and R. M. Pike.—p. 205.
Azoospermia. Congenital Absence of Vas Deferens.—p. 213.
Papillary Adenocarcinoma of Breast.—p. 215.

**Aureomycin for Pulmonary Involvement in Pancreatic Fibrosis.**—Shwachman and associates treated 35 patients with pancreatic fibrosis and pulmonary involvement with varying oral doses of aureomycin. The minimal effective dose ranged from 20 to 30 mg. per kilogram of body weight, given in one or two divided doses a day. The response was good to excellent in 31 of the 35 cases. This was characterized by disappearance of cough, improved general well-being, increased appetite and weight gain. An increase in the number and looseness of stools was noted in most patients. The drug had to be discontinued in 1 patient because of severe diarrhea. No other untoward effects were encountered. The discontinuance of the drug resulted in the prompt reappearance of symptoms. Staphylococcus aureus was isolated from the nasopharynx of all patients in this series. The clinical improvement was independent of the bacteriologic finding as determined by study of the nasopharyngeal flora. The in vitro sensitivity of the Staph. aureus isolated from these patients was determined for penicillin, streptomycin and aureomycin. The majority of strains were relatively more sensitive to aureomycin than to either of the other two antibiotics. The Staph. aureus isolated from 7 patients during aureomycin therapy showed an apparent increase in resistance ranging from four fold to thirty-two fold.

**Posterior Tuberculous Sinuses of Vertebral Origin.**—Cincotti and his co-workers show that spinal fusion continues to be the most effective method for control of the vertebral infection, while streptomycin therapy has proved extremely important in the control of the frequently associated infection of soft tissues. They are concerned with the posterior tuberculous abscess or sinus complicating Pott's disease, which interferes with the early, definitive care of the vertebral disease. In 2 of 7 cases in which wound revision with primary closure was undertaken, reformation of an abscess under the firmly healed wound occurred. When a period of continuous decompression following débridement was allowed (two to six weeks) before wound closure was undertaken, in only 2 of 26 cases was there recurrence of a sinus in the healed wound. The effectiveness of streptomycin therapy of tuberculous sinuses has been improved by the observation of the following surgical principles: superficial encapsulated tuberculous pus must be drained; the tuberculous sinus must be widely deroofed; tuberculous granulation and fibrous tissue must be removed, and extravertebral necrotic bone and cartilage must be removed. The authors report the histories of 6 patients with tuberculous spondylitis, in which spinal fusion was desirable. They describe a plan of management for the posterior tuberculous sinus of vertebral origin, stressing that streptomycin is employed in a minimal dosage through the application of established surgical principles, permitting spinal fusion to be performed early. In the good-risk patient with a meagerly draining posterior sinus, excision and immediate closure under streptomycin protection result in a firmly healed wound. Spinal fusion may then be carried out early without danger of wound contamination. In the good-risk patient with a copiously draining sinus, adequate débridement and continuous decompression over a period of days are necessary. Subsequent wound revision and secondary closure with streptomycin therapy result in a firmly healed wound. Spinal fusion is thus but slightly delayed. In the poor-risk patient with a posterior tuberculous sinus of vertebral origin, the unrestricted use of streptomycin may be necessary, but spinal fusion is possible early in the course of streptomycin therapy.

**241**:221-252 (Aug. 11) 1949

Complete Acromioclavicular Dislocation. B. M. Bosworth.—p. 221.
*Nocardiosis: Pneumonia and Empyema Due to Nocardia Asteroides. H. F. Hager, A. V. Migliaccio and R. M. Young.—p. 226.
*Orthoxine in Bronchial Asthma: Clinical Evaluation. I. W. Schiller, F. C. Lowell, W. Franklin and C. Denton.—p. 231.
Clinical Observations Concerning Schizophrenic Patients Treated by Prefrontal Leukotomy. J. L. Hoffman.—p. 233.
Exfoliative Cytology. H. Ulfelder.—p. 236.
Hemangiosarcoma of Breast.—p. 241.
Malignant Lymphoma, Hodgkin's Type.—p. 243.

**Nocardiosis.**—Hager and co-workers report 1 case of pneumonia and empyema due to Nocardia asteroides in a girl aged 16. The patient failed to respond to treatment with sulfadiazine, penicillin or streptomycin until surgical drainage of an empyema cavity and combined therapy with sulfadiazine, penicillin and streptomycin were instituted. The combined treatment apparently resulted in complete recovery, since the patient was free of symptoms and signs twelve months after discontinuance of all therapy. The patient received a total of 76,600,000 units of penicillin by intramuscular route, 10,700,000 units of penicillin intrapleurally and 288 Gm. of sulfadiazine by mouth over a period of two months. Diagnosis was established early in the course of the disease. A diagnostic thoracentesis was performed three weeks after admission to the hospital, and smears and cultures of the withdrawn fluid revealed a gram-positive, acid-fast, branching, aerobic organism identified as N. asteroides. A second strain of N. asteroides was isolated from the sputum of a woman aged 64 with bilateral apical pulmonary lesions. This organism was observed by in vitro tests to be inhibited by penicillin, streptomycin and aureomycin, but not by sulfadiazine with levels that usually can be attained clinically when adequate dosages of these antibiotics are administered. Failure to recognize N. asteroides as the causative agent in certain infections may account for the scarcity of reported cases. Such failure may be due to the way in which routine specimens of sputum are prepared for inoculation or examination. Large doses of the antibiotics to which the organism is sensitive may have to be given, and it may be necessary to administer combinations of two or more in order to obtain prompt inhibition of the organism. Surgical drainage or aspiration of loculate collections of pus is advisable for early healing. Observation for a period of years after apparent arrest of the condition is recommended.

**Methoxyphenamine Hydrochloride (Orthoxine®) in Bronchial Asthma.**—Schiller and co-workers treated 50 patients between the ages of 4 and 63 years with bronchial asthma, with methoxyphenamine hydrochloride (orthoxine®) by mouth. The dose varied from 50 mg. in children to 100 or 200 mg. in adults, given every four hours as needed. Eighteen patients had complete relief of symptoms for several hours, 17 had 50 per cent relief or more for two or more hours and 15 had unsatisfactory relief. Patients with mild asthma fared best, followed by those with asthma of moderate severity. Those with severe asthma obtained least relief. Prior to the administration of this drug 28 patients had been taking ephedrine or, having previously taken methoxyphenamine hydrochloride, had substituted ephedrine. Ten patients preferred methoxyphenamine hydrochloride to ephedrine. In 2 there was no advantage in one drug over the other, whereas the remaining 16 preferred ephedrine. In 4 patients, substitution of methoxyphenamine

hydrochloride for ephedrine was advantageous. Forty-three patients were free from any unpleasant side reaction to methoxyphenamine hydrochloride. Of the remaining 7, 4 had gastric disturbances, 1 had menstrual-like cramps, 1 reported dizziness and sleeplessness and 1 excessive perspiration. Methoxyphenamine hydrochloride is an effective oral sympathomimetic agent especially useful in mild asthma. Although it did not appear to be as effective as ephedrine, it had the advantage of causing less disturbance of the cardiovascular and central nervous systems.

## New Jersey Medical Society Journal, Trenton

**46**:313-364 (July) 1949

Pheochromocytoma: Cause of Post-Partum Convulsions. M. C. Becker, R. D. Bass and C. M. Robbins.—p. 339.
Aortic Thrombosis: Case Report. J. A. Robinson and P. H. Corrigan. —p. 343.
New Knife for Cervical Cancer. M. Joseph.—p. 345.
Verrucae Plantaris: Résumé. H. K. Schwarzfeld.—p. 347.
Bilateral Rupture of Quadriceps Tendon. R. R. Goldenberg.—p. 349.
Emotional Precipitants of Death. H. A. Davidson.—p. 350.

**46**:365-412 (Aug.) 1949

Non-Surgical Treatment of Peripheral Vascular Disorders. W. Redisch. —p. 368.
Management of Pain Associated with Disturbances of Intervertebral Disc. S. Keats.—p. 376.
Clinical Results of Use of Penicillin in Syphilis. B. Webster.—p. 380.
Cancer of Lung with Metastasis to Skin. N. J. Furst, L. Scovern and H. Quittner.—p. 387.
Malignant Melanoma. S. Roth, J. Bleiber, W. Antopol and A. Rados. —p. 388.
Pathogenesis of Atopic Eczema. W. J. Sweeley.—p. 390.
Cardiac Neoplasm Simulating Primary Heart Disease. A. Jaffin and N. Frank.—p. 393.
Exceptionally Large Twins. A. D. Summers.—p. 397.
Hydatidiform Mole of Broad Ligament: Report of Case. J. L. Flax and W. I. Weiss.—p. 398.
Vesical Neck Obstruction in Females. J. H. O'Brian and B. D. Pinck. —p. 400.

## Oklahoma State Medical Assn. Jour., Oklahoma City

**42**:273-306 (July) 1949

Medical Aspects of Atomic Energy. E. G. Williams.—p. 275.
Psychogenic Aspects of Allergy. J. A. Blue.—p. 277.
Chronic Essential Pentosuria: Report of 3 Cases. H. H. Macumber. —p. 281.

**42**:307-372 (Aug.) 1949

Newer Concepts of Digitalis Preparations. R. H. Bayley.—p. 309.
*Treatment of Syphilis by Oral Use of Aureomycin. P. A. O'Leary. —p. 315.
Contact Dermatitis. W. A. Showman.—p. 320.
Psychiatry and Medicine—One Road Ahead. C. C. Burlingame.—p. 324.
Non-Venereal Diseases of Male Genitalia. H. A. Foerster.—p. 329.
Retropubic Approach to Prostatectomy. B. H. Blocksom.—p. 331.

**Oral Use of Aureomycin in Syphilis.**—O'Leary cites factors which suggest that the future of penicillin in the treatment of syphilis may be questionable. He refers to the sensitizations and the resistance of the organisms that are appearing in increasing numbers. Animal experiments by Heilman having proved that the effect of aureomycin was several times greater against certain spirochetes than was that of penicillin, O'Leary and some of his associates started to use aureomycin in the treatment of syphilis. The drug was given orally in doses of 4 Gm. a day for a total dosage of 44 to 90.5 Gm. Two patients with early syphilis was treated with aureomycin. Treponema pallidum disappeared from the chancres in approximately 60 hours, and the cutaneous lesions involuted rapidly. Subsequently the author used aureomycin in 2 patients with late cutaneous gummas and found that the lesions involuted with the same degree of rapidity and completeness that similar lesions have involuted under heavy metal or penicillin therapy. The results of the treatment of neurosyphilis with aureomycin are not conclusive, although the tendency of the cerebrospinal fluid cell count to return to normal occurs with about the same degree of rapidity as in penicillin therapy. Oral treatment of syphilis with aureomycin is less time consuming to the patient, requires less clinical help and material, is mildly toxic and will probably become rather inexpensive in the near future. The reactions consist of nausea, vomiting and diarrhea. Evidence of sensitization from it has not been noted.

## Pediatrics, Springfield, Ill.

**4**:149-268 (Aug.) 1949

*Observations on Staphylococcal Infections Treated with Aureomycin. C. A. Chandler, E. B. Schoenbach and M. S. Bryer.—p. 149.
*Birth Injury, Focal Epilepsy and Cortical Excision: Case Report. W. Penfield and S. Livingston.—p. 157.
Streptomycin Intramuscular Dosage Per Unit Body Weight Correlated with Serum Levels in Infants and Children. A. D. Hunt Jr. and M. B. Fell.—p. 163.
Advising Parents of Early Stutterers. S. F. Brown.—p. 170.
Proteolytic Enzymes of Premature Infant with Special Reference to His Ability to Digest Unsplit Protein Food. S. Madey and J. Dancis. —p. 177.
Chronic Intussusception. H. A. Reisman and A. D. Wolk.—p. 183.
*Penicillin Therapy of Diphtheria Carriers: Analysis of 70 Cases. J. T. Y. Shen.—p. 188.
Embryoma of Kidney (Wilms' Tumor) in Children. L. B. Dickey and L. R. Chandler.—p. 197.
New Concepts of the Etiology, Diagnosis and Treatment of Congenital Megacolon (Hirschsprung's Disease). O. Swenson, E. B. D. Neuhauser and L. K. Pickett.—p. 201.
Wolff-Parkinson-White Syndrome with Congenital Heart Disease. E. E. Kleiber.—p. 210.
Mechanism of Emergence of Resistance to Streptomycin in Five Species of Gram Negative Bacilli. H. E. Alexander and G. Leidy.—p. 214.
Studies in Pancreatic Fibrosis: Simple Diagnostic Gelatin Film Test for Stool Trypsin. H. Shwachman, P. R. Patterson and J. Laguna. —p. 222.
Bronchiectasis in Childhood: II. Aetiology and Pathogenesis, Including a Survey of 272 Cases of Doubtful Irreversible Bronchiectasis. C. E. Field.—p. 231.
Systemic Infection with Salmonella Anatum: Report of First Case. Chieh Sung, J. Fournier and Siang-Yuen Chang.—p. 249.

**Aureomycin in Staphylococcic Infections.**—Chandler and co-workers used aureomycin in 5 newborn infants and 1 child aged 17 months with staphylococcic infections, who had shown no clinical response to penicillin and sulfadiazine. Two of the patients had breast abscesses, 2 had cellulitis, 1 had staphylococcic pneumonia and the 17 month old child had staphylococcic septicemia. The 5 newborn patients were given by mouth 60 mg. of the drug per kilogram of body weight. The patient with staphylococcic pneumonia was given an additional 20 mg. per day intramuscularly because of the severity of his infection. The patient with staphylococcic septicemia was given 100 to 600 mg. by mouth and 160 mg. intramuscularly per day. Aureomycin was administered for a mean period of ten days; the shortest period was three days and the longest seventeen. No exacerbations of fever or of infectious lesions were noted in any case after therapy had been discontinued. The response of the newborn infants to the administration of the drug was highly satisfactory. There was decided clinical improvement in all patients within forty-eight hours. In the patient with staphylococcic pneumonia, within forty-eight hours not only was there roentgen evidence of resolution of the pneumonia but even the nose and throat cultures had become sterile. Only 1 patient required incision and drainage of the breast abscess on the fifth day of therapy, but the lesion had completely localized by that time. The critically ill patient with septicemia, probable peritonitis and liver abscess had one positive blood culture on the fifth day of aureomycin therapy, but thereafter his blood cultures remained sterile, his symptoms rapidly disappeared and he made an uneventful recovery. Except for mild vomiting and a few loose stools aureomycin was well tolerated.

**Birth Injury, Focal Epilepsy and Cortical Excision.**—Penfield and Livingston report 1 case of a brain injury at birth in a boy now aged 8 years. There was no history of epilepsy or convulsions of other members of the family. He vomited several times two days after birth and had two generalized convulsions. Vomiting and three more convulsions occurred within the subsequent two days. He was given vitamin K and treated symptomatically. He held up his head at 3 weeks and sat alone at 4 months, and his mental development seemed to be normal until he reached 6 months of age. Recurring cerebral seizures began at 5 months, and soon thereafter there was decided deterioration. He could not hold up his head and became completely apathetic. He was treated with phenobarbital, bromides and diphenylhydantoin sodium with little benefit. Roentgenographic examination of the skull showed that the right cranial chamber was smaller than the left. Preoperative encephalography gave evidence of a focal epileptogenic lesion in the right hemisphere in the vicinity of standard head position C6. At the age of 12 months the patient was subjected to a large right-sided osteoplastic craniotomy with removal of narrow, tough gyri bordering

a fluid-filled space adjacent to and within the frontal lobe. The simple excision of these half-destroyed gyri resulted in cessation of seizures. It terminated the deterioration of the infant and permitted resumption of more or less normal development. The patient has now a chronologic age of 8 years and 4 months, a mental age of 6 years and 2 months and an intelligence quotient of 69 per cent. Birth trauma may produce a local cerebral lesion which is relatively unimportant until it ripens into the epileptogenic focus, from the generalized influence of which intellectual and behavioral deterioration may sometimes result. This ripening process may require six months to twenty years.

**Penicillin for Diphtheria Carriers.**—Shen treated 70 diphtheria carriers, 37 male and 33 female subjects, most of them between 5 and 14 years old, with penicillin. Intramuscular treatment with 30,000 units of penicillin every three hours was effective in getting three daily consecutive negative cultures after discontinuation of the treatment. The average clearing time was 4.9 days. The average clearing time for those treated with intramuscular and local penicillin was 6.3 days. In the 11 patients treated with procaine penicillin, the average clearing time was 4.0 days. Although the incidence of enlarged tonsils in this group was lower than that of the other groups, the good results could be due to the larger dosage and more sustained level of the procaine penicillin. Five carriers received local treatment alone, with a clearing time of 7.0 days. The average clearing time for carriers with normal, enlarged, and enlarged cryptic tonsils was 5.6, 6.4 and 16.4 days, respectively. Carriers with a clearing time of more than five days showed a much lower percentage of normal tonsils and a much higher percentage of inflammation than the group with a clearing time of less than five days. These observations suggest that there is a definite relationship between the incidence and degree of the pathologic condition of the throat and the response to penicillin treatment. Intramuscular penicillin is highly effective in simple cases of diphtheria carriers. Five thousand units per pound of body weight per day for five days seems to be curative. Procaine penicillin is preferable because of its convenience of administration and its more sustained level. Local sprays or nose drops can be employed along with parenteral therapy. A solution with 10,000 units per cubic centimeter is recommended. Serious nose or throat pathologic conditions should be corrected surgically after one or two days of penicillin administration. In cases that have recurred without any nose or throat pathologic condition, a sensitivity test of the organism should be done and the dosage of penicillin adjusted. Two consecutive daily negative nose and throat cultures are necessary for discharge. A separate nose and throat culture should be taken one week after discharge for check-up purposes.

## Philippine Medical Association Journal, Manila

**25**:259-332 (June) 1949. **Partial Index**

Use of Male Philippine Rana Vittigera Wiegmann in Diagnosis of Pregnancy. F. C. Bocobo, I. Lawas, G. T. Aragon and J. Silva.—p. 259.
Biochemical Studies on Tuberculosis: VII. Sedimentation Rate as Index of Protein Deficiency Rather than of Infectious Activity in Tuberculosis. J. F. Leyva.—p. 267.
*Extract of Wings of Philippine Butterfly, Terias Hecabe Linnaeus, New Antibiotic for Malaria. E. Y. Garcia.—p. 279.
Protecting Eyesight in Philippine Industry. J. S. Santillan and A. A. Gorospe.—p. 307.

**Extract of Butterfly Wings for Malaria.**—Garcia cites evidence to the effect that para-aminobenzoic acid is essential for the growth of malarial parasites and reasons that the presence of any substance capable of inhibiting the action of this acid can disturb the growth of the plasmodia. The antimalarial effect of sulfonamide drugs, for instance, seems to be due to its antagonistic action toward para-aminobenzoic acid. The action of sulfonamide drugs is indirect or antibiotic rather than parasiticidal. The author tried "hecabepterin," a pure extract of the wings of the Philippine butterfly (Terias hecabe Linnaeus), on malaria patients. After preliminary trials, which indicated that a more concentrated extract of hecabepterin was necessary, Garcia describes observations which indicate that the para-aminobenzoic acid was either destroyed or inhibited by the extract, resulting in the disappearance of the erythrocytic parasites. This treatment was tried on 30 human subjects, selected for having had relapsed infections. These subjects included 16 with infection caused by Plasmodium vivax, 10 with Plasmodium falciparum infection and 4 with Plasmodium malariae infection. The average rates of decrease in parasite counts in infections with P. vivax and P. malariae were 52 and 45 per cent respectively, compared with their corresponding controls, while that in infection with P. falciparum was 74 per cent that of its control. Apparently the extract of butterfly wings, hecabepterin, exerts an antibiotic effect on malarial parasites. This is the first time in this age of antibiotic therapy for bacterial organisms that an antibiotic has been found for a hemoprotozoan parasite. The insect world seems to be another possible source of antibiotics for bacteria and protozoa.

## Southern Medical Journal, Birmingham, Ala.

**42**:635-730 (Aug.) 1949

Corrosive Strictures of Esophagus and Their Treatment. M. G. Lynch.—p. 635.
Complications of Glaucoma Surgery. P. M. Lewis.—p. 640.
Epidermolysis Bullosa Hereditaria. R. G. Thompson, C. L. Leedham and H. Hailey.—p. 647.
Correlative Studies of Testicular Dysfunction. J. Hayman.—p. 653.
Gangrene of Penis Following Circumcision with High Frequency Current: Plastic Reconstruction of Penis. W. G. Hamm and F. F. Kanthak.—p. 657.
Serial Needle Biopsy in Study of Hepatic Disease. J. S. Levy, E. L. Wilbur, G. Bozalis and others.—p. 659.
Hepatic Failure: Emphasis on Water Balance. C. M. Caravati and J. M. MacMillan.—p. 666.
Effects of Lipotropic Substances on Phospholipide Synthesis in Patients With and Without Chronic Hepatitis as Measured by Radioactive Phosphorus. D. Cayer and W. E. Cornatzer.—p. 669.
Vitamin $B_{12}$ in Pernicious Anemia. M. F. Beard, M. Nataro and L. H. Layman.—p. 677.
Current Concepts in Control and Treatment of Intestinal Parasites W. L. Treuting.—p. 684.
Emergency Treatment of Fractures. P. B. Wright.—p. 687.
Use of Wire Sutures in Compound Wounds. R. H. Bell.—p. 691.
Herpes Zoster: Treatment with Chloramphenicol. L. M. Dawson and H. E. Simon.—p. 696.
Insulin Resistance: Survey of Literature and Report of 2 Cases. N. Burnstein and McL. Patterson.—p. 697.
Rectal Disorders and Nervous Patient. R. C. Alley.—p. 703.
Therapy in Private Practice of Psychiatry. L. F. Woolley.—p. 707.
Cerebral Allergy. H. M. Davison.—p. 712.
*Vitamin E.: Therapeutic Perpetration. H. Eichert.—p. 717.
*Relief of Symptoms of Acute Gout and Rheumatoid Arthritis by Means of Pituitary Adrenocorticotropic Hormone (ACTH). T. D. Spies and R. E. Stone.—p. 720.

**Vitamin E, a Therapeutic Perpetration.**—Eichert reviews the status of vitamin E and alpha-tocopherol in the treatment of cardiovascular disease. He shows that this substance came into widespread use in 1946, after the publication of extravagant claims by Shute and Vogelsang. Although this group of investigators and their disciples have continued to report fabulous success in the treatment of almost every known type of cardiovascular disorder, all other authors who have investigated this treatment find it to be worthless. In spite of the dubious value of this drug, its widespread use continues. The perpetration of this nostrum on a gullible public is a reflection of the influence which lay publications exert on medical practice. A small group of physicians were able, by presenting their opinions to the public through the lay press before these had been corroborated, to force thousands of other physicians to treat heart disease with vitamin E. Eichert stresses that there is great need for wider publication of studies and comment on the true value, if any, of vitamin E in heart disease, to combat the unsupported claims for this product which are being widely disseminated in lay publications and trade journals.

**Pituitary Adrenocorticotropic Hormone in Gout and Arthritis.**—Spies and Stone feel that the work of Hench, Kendall, Slocumb and Polly in showing that 14 patients with rheumatoid arthritis were relieved by treatment with the compound E (the adrenal cortical hormone, 17-hydroxy-11-dehydrocorticosterone) and 2 patients by treatment with pituitary adrenocorticotropic hormone, marks a milestone. They themselves have been studying the effects of various nutrients and hormones on the diseases of later life. Since pituitary adrenocorticotropic hormone (ACTH) stimulates the adrenals to make compound E, they recently have administered adrenocorticotropic hormone to a patient with severe gout and to 3 patients with moderately severe rheumatoid arthritis. They found that the administration of this agent to a patient with advanced deforming gouty arthritis was followed by disappearance of pain in the knee joint and the great toe. The reddish purple of the great toe disappeared, and the swelling decreased by 25 per cent within a few hours. The

administration of adrenocorticotropic hormone to 3 patients with rheumatoid arthritis was followed by great symptomatic and objective improvement. The amount of the drug available was not sufficient to permit its use indefinitely, so that the administrations were of necessity discontinued. Adrenocorticotropic hormone is not a cure for gout or rheumatoid arthritis. However, its relief of symptoms and subsequent objective changes were more profound than any the authors have seen following the use of any other form of therapy.

## Surgery, Gynecology and Obstetrics, Chicago

**89**:129-256 (Aug.) 1949


*Surgical Correction of Constrictive Pericarditis. E. Holman and F. Willett.—p. 129.
Bronchiectasis: Study of Segmental Distribution of Pathologic Lesions. J. R. Moore, S. D. Kobernick and F. W. Wiglesworth.—p. 145.
Vagovagal Reflexes: Electrocardiographic Changes During Vagotomy. M. J. Gullickson, J. H. McRae and D. A. Campbell.—p. 153.
Effect of Pancreatic Juice on Gall Bladder. S. E. Reid.—p. 160.
Morbid Factors in Experimental Appendicitis. C. A. Tanturi and R. E. Anderson.—p. 165.
Blood and "Available Fluid" (Thiocyanate) Volume Studies in Surgical Patients; Part II. Operative and Postoperative Blood Loss with Particular Emphasis upon Uncompensated Red Cell Loss. J. R. Stanton, R. P. Lyon, E. D. Freis and R. H. Smithwick.—p. 181.
Vaginal Hysterectomy. E. A. Edwards and R. A. Beebe.—p. 191.
Experimental Thoracic Duct Fistula: Observations on Technique, Absorption of Fat and Fluid from Intestine, and Protein Depletion. W. W. L. Glenn, S. L. Cresson, F. X. Bauer and others.—p. 200.
*Ewing's Tumor. B. McSwain, B. F. Byrd Jr. and W. O. Inman Jr. —p. 209.
Posterior Subsphincteric Space: Its Relation to Posterior Horseshoe Fistula. H. Courtney.—p. 222.
Criteria, Classification and Technique of Iliopectineal (Cooper's) Ligament Hernioplasty. C. C. Burton.—p. 227.
Superficial Lobectomy and Total Parotidectomy with Preservation of Facial Nerve in Treatment of Parotid Tumors. D. State.—p. 237.


**Surgical Correction of Constrictive Pericarditis.**—According to Holman and Willett the operation for chronic constrictive pericarditis has yielded varying results, some disappointing and some spectacularly brilliant. They review 265 cases reported in the literature, cite experiences and suggestions made by different surgeons and report their own observations. Of 9 patients operated on by them 5 had pericarditis of unknown causation; of the 5, 1 died, 3 were cured and 1 improved. The other 4 had active tuberculous pericarditis. Of these, 2 were cured and 2 improved. In 265 recorded operations for constrictive pericarditis, 22 deaths occurred on the operating table and 48 in the early postoperative period; 118 patients were considered cured and 44 improved. The following factors contributed to the success of the operation: its application in young persons in whom other organs were normal and in whom liberation of the compressed heart or its vessels was the only correction necessary; the availability of intratracheal anesthesia and of oxygen, transfusions and antibiotics; adequate exposure of the heart, permitting ready access to critical areas for removal of the offending scar; the operating surgeon's courage and technical skill, which enabled him to pursue the operation until adequate decompression of all critical areas had been achieved. Contributing to poor results were tuberculous or pyogenic etiologic factors; operation on exceedingly ill patients; technical difficulties such as tears in the thin-walled auricle or in the myocardium of the right ventricle; inability to remove the scar because of penetration of cardiac musculature by calcium deposits; failure to remove the scar over critical areas such as the inferior and superior vena cava; technical difficulties imposed by inadequate exposure of the heart, and, last, delay in correct diagnosis until the liberation of attenuated and atrophied myocardium resulted only in circulatory failure. To achieve the exposure necessary for an adequate inspection and decortication of the heart, a median sternotomy with transverse division of the sternum in the second interspace is recommended.

**Ewing's Tumor.**—McSwain and associates report the apparent cure of 3 patients with Ewing's tumor (angioendothelioma) of the bone and summarize the features of the 20 cases of this disease which were seen at the Vanderbilt University Hospital since 1925. Thirteen of the 20 cases were in males. The ages of the 20 patients varied between 3 and 43 years. The periods which had elapsed from the onset of symptoms until the application for treatment ranged from five weeks to twelve months. In 10 patients there was no history of injury, while in the other 10 there was. Pain and swelling was noted in practically all instances. The authors found the tumors more frequently in flat bones (14 cases) than in long tubular bones (6 cases). This contradicts the observations of Ewing, Geschickter and Copeland, but corroborates those of Stout, Lichtenstein and Jaffe. In most instances the tumors were visible and in all patients they were palpable. Most of the tumors were smooth, and all were firm or hard, and immovable. None was fixed to the skin. The roentgenologic observations in these patients were so variable that the diagnosis of Ewing's tumor was made by the roentgenologist in only 5 of the cases which occurred in the flat bones and in none of those which occurred in the long bones. It is impossible to make an unequivocal diagnosis of this disease by the roentgenogram alone. All such lesions should be subjected to exploration and removal of tissue for microscopic examination. When Ewing's tumor is suspected no patient should be subjected to irradiation or amputation until microscopic examination of excised tissue has confirmed the diagnosis. It has been possible apparently to cure this disease in 1 instance by amputation, in another by irradiation and in a third by irradiation and amputation. Two instances were recorded in which, without direct treatment, apparent pulmonary metastases from Ewing's tumor disappeared.

## United States Naval Med. Bulletin, Washington, D. C.

**49**:617-824 (July-Aug.) 1949. **Partial Index**


Treatment of Pulmonary Tuberculosis: Evaluation of Present Methods. E. Ricen.—p. 617.
Experiences with Marrow Nail Operation According to Principles of Kuentscher: Fresh Compound Fractures. Part II. C. Haebler.—p. 626.
Psychiatric Rehabilitation: Follow-Up Study of 200 Cases. D. S. Smith and M. E. Hawthorne.—p. 655.
Urinary Extravasation Proximal to Triangular Ligament: Method of Repair. J. T. Mason and R. K. Ratliff.—p. 670.
Routine Sigmoidoscopy: Review of 300 Consecutive Examinations. H. M. Wertheimer.—p. 681.
Malignancies of Sigmoid Colon. L. L. Bean.—p. 685.
Fulminant Epidemic Hepatitis: Report of Case in Infant. R. M. Dimmette.—p. 699.
Leukonychia Totalis: Review and Report of Case. J. G. Stubenbord 3d. —p. 710.
Acute Virus Hepatitis. H. A. Weiss.—p. 713.
Pyloric Stenosis in Binovular Twin Boys. A. S. Chrisman and T. Loizeaux.—p. 727.
Congenital Talipes Equinovarus: Treatment with Modified Denis Browne Splint. R. E. Kendrick.—p. 730.
Plastic Repair of Surface Defects in Preparation for Bone Grafting. O. W. Wickstrom.—p. 736.
*Pathology of Acute Alcoholism. W. O. Umiker.—p. 744.
Method for Serum Albumin Determination. A. F. Braff and J. M. Cobb. —p. 753.
Field Trial of "Shigella Flexneri III" Vaccine: Background, Scope and Organization of the Program. L. A. Barnes, I. L. Bennett Jr. and R. S. Gordon.—p. 757.
Some Recent Advances in Aviation Medicine. H. G. Shepler, H. A. Smedal and R. L. Christy Jr.—p. 775.


**Pathologic Basis of Acute Alcoholism.**—According to Umiker fatal, uncomplicated, acute poisoning due to alcohol is uncommon. Only 3 cases were found in a series of well over 1,000 unselected necropsies at the U. S. Naval Hospital, Bethesda, Md. These cases are reported. It is not easy to consume a dose of alcohol that will prove fatal. In the usual bout of heavy drinking the participant loses consciousness, and thereby the ability to consume more alcohol, before a lethal dose is taken. Nevertheless, acute alcholism with its resultant physical, mental, emotional and moral deterioration is the underlying factor in a large percentage of deaths: The drunken pedestrian stumbles in front of a bus; the intoxicated driver falls asleep at the wheel; the emotionally disturbed drinker takes his or another's life; the circulation in a stenosed coronary artery falters under the strain of acute alcoholism, or the pneumococcus finds an easy victim. The pathologist often fails to consider the possibility of acute alcoholism, and the final diagnosis is made by the toxicologist rather than by the pathologist. The most constant pathologic changes are severe meningeal and cerebral congestion, pulmonary edema, acute gastritis, visceral congestion and acute pancreatic necrosis. Most of these changes are found in other conditions, especially those characterized by anoxemia. Postmortem blood, urine and tissue alcohol determinations are of diagnostic value only when death has taken place within a few hours after the onset of the alcoholic coma. Acute alcoholism should be suspected in all cases of suicide, homicide, accidental trauma and poisoning and as a complicating or precipitating factor in other medical or surgical fatalities.

## FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

### British Journal of Radiology, London

**22**:415-496 (Aug.) 1949. **Partial Index**

SYMPOSIUM—DIVERTICULA OF ALIMENTARY TRACT

Diverticula of Oesophagus. A. S. Johnstone.—p. 415.
Radiological Aspects of Diverticula of Stomach and Small Bowel. R. Fawcitt.—p. 427.
Diverticulosis and Diverticulitis of Large Intestine (Radiological Commentary). J. L. A. Grout.—p. 442.
Synchrotron Accelerator—Its Potentialities as Generator of X-Rays and Electrons of 10-50 MeV Energies for Medical Use. D. W. Fry. —p. 462.
Microwave Linear Electron Accelerator. G. R. Newbery.—p. 473.

### British Medical Journal, London

**2**:297-346 (Aug. 6) 1949

Tuberculosis: Certain Unexplained Mortality Figures. W. Elliot.—p. 297.
Problems of Ageing and Chronic Sickness. A. P. Thomson.—p. 300.
Return to Work of Elderly Male Hospital In-Patients. J. Pemberton and J. C. Smith.—p. 306.
Broncho-Pulmonary Segments of Lung and Their Terminology. J. Hardie-Neil and W. Gilmour.—p. 309.
*"Tridione" in Treatment of Epilepsy. C. W. M. Whitty.—p. 311.
*Use of "Tridione" in Petit Mal. F. C. Haward.—p. 315.
Case of Salmonella Enteritidis Septicaemia with Lung Abscess. I. McL. Baird and L. Capper.—p. 316.

**Trimethadione (Tridione®) in Epilepsy.**—Of the 50 patients treated with trimethadione by Whitty, 22 had the petit mal type, 24 had mixed grand and petit mal, 3 had grand mal only and 1 had a unilateral tremor-rigidity syndrome. The petit mal attacks were abolished or decidedly lessened in 31 cases, they were reduced in 10 and unaffected in 5. Grand mal was reduced in 5 cases, unchanged in 9 and aggravated in 10, in 1 of which status epilepticus occurred. Evidence of serious though transient toxic effects on the blood was shown in 2 cases. Other toxic effects included "glare," rashes, irritability, hiccup, drowsiness and ataxia. Except for the first two, these were unusually slight or transient. The drug was discontinued in 8 cases because it was ineffective or too provocative of grand mal, in 3 because improvement was maintained without it and in 1 because of pronounced irritability.

**Trimethadione (Tridione®) in Petit Mal.**—Haward says that, since he knew little of the possible toxic effects of trimethadione, the trial was limited to 50 cases, but he feels that these were sufficient to permit assessment of the efficacy of the drug. The patients were chosen at random; some had petit mal alone and some petit mal with grand mal. He concludes that trimethadione is of value only in the treatment of petit mal. An analysis of the effects of treatment on adults and children indicate that the best results were obtained in children.

### Journal Obst. & Gynaec. of Brit. Empire, Manchester

**56**:341-528 (June) 1949. **Partial Index**

Rubella in Pregnancy as Aetiological Factor in Congenital Malformation, Stillbirth, Miscarriage and Abortion. C. Swan.—p. 341.
Haemangiomata of Pregnancy. T. F. Rose.—p. 364.
Schistosomiasis in Gynaecology. G. P. Charlewood, S. Shippel and H. Renton.—p. 367.
*Foetal Mortality in Postmaturity. J. M. McKiddie.—p. 386.
Establishment of Extra-Uterine Respiration. J. E. Morison.—p. 393.
Observations on Human Leucocytes During Menstrual Cycle. I. L. MacKinnon.—p. 404.
Tuberculous Ulceration of the Vulva (with Report of One Case Successfully Treated with Streptomycin). A. G. Mathew.—p. 408.
Foetal Mortality of Toxaemia of Late Pregnancy According to Mode of Delivery. J. Hamilton, T. N. A. Jeffcoate and U. M. Lister.—p. 413.
Torsion of Ovarian Cyst in Young Child. J. Cook.—p. 430.
Surgical Induction of Labour. H. J. D. Smythe.—p. 431.
Virilism and Theca-Cell Hyperplasia of the Ovary: A Syndrome. A. Culiner and S. Shippel.—p. 439.

**Fetal Mortality in Postmaturity.**—McKiddie reasons that, if postmaturity itself could cause fetal death before the onset of labor, then it might be assumed that it could also weaken the fetus, thus predisposing to fetal distress or death during the course of labor. To discover how often fetal death might be attributed to postmaturity, the records of all cases at the Aberdeen Maternity Hospital were examined for the years 1940 to 1944 and for 1946. In this series prolongation of pregnancy was the sole criterion of postmaturity. Births were regarded as premature if labor took place more than seven days before the expected date of delivery; full term: seven days before to seven days after the expected date of delivery; postmature: more than seven days beyond the expected date of delivery. If dates were doubtful, as was the case in 1,211 of a total of 8,014 deliveries, the deliveries were excluded from this study. Of the remaining 6,803 deliveries, 1,795 were premature, 3,366, or nearly half, were full term and 1,642 postmature. Reviewing experimental physiologic work the author finds that in postmaturity the fetus increases in size as it becomes postmature; oxygen saturation of the circulating fetal blood gradually diminishes, and at term the efficiency of the maternal uterine circulation becomes impaired. Although compensatory fetal mechanisms exist, these are not adequate in the large postmature fetus to counterbalance the impaired maternal circulation. This is shown by the diminution of oxygen saturation in the blood of the postmature fetus. Prolonged exposure to such conditions would lead to fetal asphyxia in utero. Analysis of cases in the Aberdeen Maternity Hospital suggests that the proportion of stillbirths is higher in postmature infants than in infants at term; the percentage of stillbirths rises with the degree of postmaturity; the unexplained stillbirth figure rises with degree of postmaturity; fetal distress is more common in postmature babies and seems to be related to degree of postmaturity.

### Lancet, London

**2**:225-264 (Aug. 6) 1949

Chronic and Unexplained Oedema. A. G. W. Whitfield and W. M. Arnott.—p. 225.
*Conservative Treatment of Anuric Uraemia. G. M. Bull, A. M. Jockes and K. G. Lowe.—p. 229.
Removal of Simple Univesicular Pulmonary Hydatid Cyst. N. R. Barrett.—p. 234.
Diurnal Variation in Fat Content of Breast-Milk. M. Gunther and J. E. Stanier.—p. 235.
Sloughs of Tracheal Mucosa. F. L. Turner.—p. 237.
Megaloblastic Anaemia in Coeliac Disease Treated with Folic Acid. M. L. Thomson, H. W. Dalton and V. K. Wilson.—p. 238.
Volvulus of Caecum Presenting as Strangulated Inguinal Hernia. H. D. Moore.—p. 240.
*Fatal Coronary Occlusion in Girl Aged 16. W. G. MacDougall.—p. 241.

**Conservative Treatment of Anuric Uremia.**—Bull and his associates feel that from the therapeutic point of view two types of uremia should be differentiated: one in which the kidney can excrete water but cannot maintain normal internal conditions without special management and the other in which negligible quantities of water are excreted. It is this latter group, the anuric uremias, with which they are primarily concerned. Their regimen is based on accurate control of water, mineral and nitrogen balance. Through a stomach tube, which is passed through the nose, the following mixture is dripped at a steady rate: 400 Gm. of dextrose, 100 Gm. of peanut oil, sufficient acacia to emulsify the mixture, vitamins if desired and 1 liter of water. All vomit is collected, filtered and returned to the stomach. This insures that the fluid intake is accurate and that there is no loss of food or electrolytes. When diuresis starts, difficulties in management arise, because the kidney recovers its electrolyte-regulating function slowly. Urinary losses of the various electrolytes must be made good. To the basic intake of 1 liter of water, fluid is added daily in a volume equal to the urine passed during the preceding twenty-four hours. The drip feeding should be discontinued and superseded by a low protein diet when the urine output exceeds 1 liter a day. Because anemia leads to diminished renal function, fresh packed red cells are given by transfusion if the hemoglobin concentration is below 70 per cent. The effect of this regimen was observed in controls without renal disease, in patients with reduced renal function but without anuria and in patients with anuric uremia. The authors treated 11 patients with extreme oliguria or anuria lasting seven to twenty-one days. Four of these 11 patients died; 2 of these were already comatose on admission and died within twenty-four hours. The other 7 patients survived and left the hospital symptom free and with adequate renal function. The authors believe that the high carbohydrate content of this diet is important and that the effectiveness of the regimen is not entirely due to its nitrogen-sparing effect but that collateral effects on mineral balance are

of equal or greater importance. Dialysis should not be undertaken where this regimen is started early. However, dialysis probably has a place in the treatment of patients who are in gross water, mineral and nitrogen imbalance. Methods such as splanchnic block, spinal anesthesia and decapsulation of the kidney are of doubtful value. If conservative management is instituted early without previous overhydration, diuresis can be confidently anticipated in anuria due to any recoverable renal lesion. Recovery may be delayed; in 1 patient it took place after more than three weeks' extreme oliguria.

**Fatal Coronary Occlusion in a 16 Year Old Girl.**—MacDougall reports the case of a 16 year old girl who had been well until fourteen days prior to examination, when on hurrying home from work she suddenly experienced shortness of breath associated with a gripping pain extending widely across the front of the lower part of the chest and upper part of the abdomen. With rest both pain and breathlessness were relieved. Thereafter these symptoms recurred daily whenever she hurried, and relief was always obtained with rest. On the tenth day after the onset she consulted her doctor but did not accept his advice to rest in bed. That evening she was more breathless than usual but obtained complete relief when she went to bed. In the early hours of the following morning she woke with gross dyspnea and severe pain in the middle of the sternum. These symptoms continued during the following thirty-six hours, during which she also had bouts of vomiting. She was then admitted to the hospital; her condition rapidly deteriorated and she died twenty-four hours after admission. Autopsy revealed a large infarct, ten to fourteen days old, which involved the lower part of the interventricular septum, the anterior part of the apexes of the left and right ventricles and the posterior part of the left ventricle. In the upper part of the posterior wall of the left ventricle, toward the base, an extensive area of fibrosis indicated a previous myocardial infarction. This earlier infarct appears to have developed without the classic symptoms, nor did its presence have any adverse effect on physical activity before the onset of the terminal illness. The small area of arterial necrosis, which was considered too pronounced to be purely a response to the thrombosis, was probably true arteritis and responsible for initiating the thrombosis.

## Archivos Argentinos de Pediatría, Buenos Aires

**20**:263-330 (June) 1949. **Partial Index**

*Complex Malformation: "Situs Inversus" with Levocardia and Congenital Heart Disease and Cystic Disease of Lung. M. J. Del Carril, R. Kreutzer, J. R. Vásquez and A. R. Albanese.—p. 263.
Penicillin in Diphtheria. F. Bazán, E. Schteingart and L. Rodríguez Gaeta.—p. 296.

**Complicated Visceral Abnormalities.**—The subject of this report is a 21 month old girl with cyanosis from birth. There was neither tuberculosis nor syphilis in the history of the family. The mother and older brother of the patient had congenital aniridia. At the age of 21 months the patient suddenly presented left hemiparesis. Examination of the patient revealed transposition of the viscera, levocardia, cardiopathy and cystic disease of the lung. Pneumonectomy was performed on the assumption that hemiparesis was caused by an embolus from the cystic lung. This was followed by improvement in the blood, and almost complete disappearance of cyanosis and of the cardiorespiratory difficulties. The patient was well as of the time of reporting, one year and three months after the operation. The auricles were not transposed, notwithstanding the fact that the inferior vena cava followed an abnormal course on the left side of the stomach.

## Arquivos de Neuro-Psiquiatria, São Paulo

**7**:113-238 (June) 1949. **Partial Index**

*Prefrontal Lobotomy. Clinical Results in a Private Hospital. P. W. Longo, A. Mattos Pimenta and J. Arruda.—p. 126.

**Prefrontal Lobotomy.**—Longo and collaborators performed prefrontal lobotomy in 21 adult patients in a private psychiatric hospital. Complete recovery was obtained in 6 patients, all of whom had had the disease for one to four years prior to operation. Nine patients were improved. The operation failed in 6. Best results were obtained in patients in whom the disease had been of short duration. Chronic anxiety and paranoid schizophrenia are more easily controlled, provided the disease is not of long duration. There were no fatalities, immediate or late complications or aggravation of the disease. The operation is of value, especially in patients with a tendency to chronicity. The earlier the operation in the course of the disease, the better the preservation of the intellectual level of the patient before the operation and the more satisfactory the results.

## Deutsche medizinische Wochenschrift, Stuttgart

**74**:893-940 (July 29) 1949. **Partial Index**

Structural Analysis of Psychoses in Feebleminded Patients. K. Schneider.—p. 893.
Complications in Artificial and Spontaneous Pneumothorax. F. Lommel—p. 895.
*Leptospiral Diseases with Aspects of So-Called Idiopathic and Abacterial Meningitis. W. Scheid.—p. 898.
Acute Forms of Jaundice. W. Siede.—p. 901.
*Cholecystopathy Following Gastric Resection, with Special Consideration of Cholecystopathy Associated with Duodenal Ulcer. H. Hoerstke.—p. 905.
Vitamin E and Carbohydrate Metabolism. H. A. Heinsen.—p. 908.
Injury of Leukocytes by Medication with Urethane. S. Sandküler and I. Wagner.—p. 912.

**Leptospiroses with Aspects of Abacterial Meningitis.**—Scheid points out that Wallgren, in 1925, described a form of meningitis which he identified as acute aseptic meningitis. Subsequent reports by numerous other investigators frequently designated this process as benign lymphocytic meningitis. Scheid feels that the terms "aseptic" and "abacterial" can be misleading, because the terms indicate only that no organism can be detected with the customary microscopic and cultural methods. Aseptic or abacterial meningitis is really not an entity but a syndrome that may have various causes. In some cases, epidemiologic considerations may indicate a poliomyelitis process. The virus or epidemic parotitis likewise may cause meningitis and in some of these cases the typical symptom of parotitis is absent. Infectious mononucleosis also has been known to be associated with symptoms of abacterial meningitis. The author cites cases which demonstrate that leptospiral infection may present features of abacterial meningitis. Serologic studies indicated infection with Leptospira canicola or with Leptospira icterohaemorrhagiae, and epidemiologic inquiries disclosed contact with diseased dogs. Contradictory statements regarding the frequency of meningitic symptoms in leptospiral infections are probably largely due to the fact that examinations of the cerebrospinal fluid were not done. The assumption that the meningitic form of leptospiroses represents a special complication canont be defended. It is more probable that, as in syphilis, there is frequently, if not regularly, an infection of the meninges, which is not necessarily reflected in the cerebrospinal fluid. Changes in the cerebrospinal fluid may persist long after other meningitic symptoms have subsided. The sedimentation reaction suggests that leptospirae may persist in various organs, including the meninges. The meningitic disturbances produced by leptospiral organisms are frequently atypical, and only serologic studies can verify the diagnosis. The possibility of a leptospiral infection should be taken into consideration in all cases of abacterial meningitis.

**Cholecystopathy and Duodenal Ulcer.**—Hoerstke comments on the frequent association of cholecystopathy and duodenal ulcer. He encountered cholecystopathy in 54 of 138 patients with chronic relapsing duodenal ulcer. In a table which lists data on 96 patients who underwent various operations on the stomach, he shows that the incidence of cholecystopathies is much greater in patients who underwent surgical treatment for duodenal than for gastric ulcers. Many of these patients had cholecystopathy before the operation. The factors that presumably are responsible for the persistence or new development of cholecystopathy following resection for duodenal ulcer include: dyskinesia in patients with duodenal ulcer; ascendance of the bacterial flora of the colon to the duodenum, with possible infection; inadequate stimulation of the liver and pancreas, because of the abolishment of duodenal passage for food; stasis in the gallbladder, and impairment of digestion in the small intestine with its sequels. To reduce the incidence or the severity of biliary disturbances it is essential to continue the dietetic treatment after gastric resection, the use of choleretics and other measures usually available in spas.

## Harefuah, Jerusalem-Tel Aviv

**37**:25-36 (Aug. 1) 1949

*Transpleural Drainage of Tuberculous Cavities. P. Wayl and J. Rakower. —p. 27.
Drainage by Monaldi's Method and Thoracoplasty. K. Friedmann.—p 29.
Streptomycin in Subacute Bacterial Endocarditis with Blood Cultures of Anaerobe Streptococcus of the Veillonella Group. L. Ascher.—p. 31.

**Transpleural Drainage.**—According to Wayl and Rakower, transpleural drainage should be practiced to aid the healing of tension cavities and of giant cavities and occasionally only as symptomatic treatment. Temporary improvement may be obtained with transpleural drainage in most cases, but improvement disappears as soon as the drainage is discontinued. Definite cicatrization of the cavity results rarely from transpleural drainage alone. The main purpose of transpleural drainage is to prepare the patient for thoracoplasty by detoxication. Transpleural drainage should be practiced as long as possible in cases in which thoracoplasty is not feasible. There is a noteworthy difference between immediate and distant results of transpleural drainage. In their immediate results the authors noted an improvement in more than 50 per cent of the cases; no results were obtained in one third of the cases and in 10 per cent there was deterioration. Distant results showed recovery in 14.3 per cent of the cases and improvement in 28.5 per cent, while in 42.9 per cent there was no change and in 14.5 per cent there was deterioration. This difference may be attributed to the fact that closure of a draining bronchus in the drained cavity occurs in exceptional cases only. The cavity reopens frequently after drainage is discontinued.

## Presse Médicale, Paris

**57**:753-764 (Aug. 20) 1949

*Synergic Association of Streptomycin and Sulfadiazine in Treatment of Human Brucellosis Due to Brucella Melitensis. M. Janbon and L. Bertrand.—p. 753.
*Electroshock as Method of Treatment for Intractable Pain; Causalgia, Refractory Neuralgia, Pains of Morphine Addicts and Subintrant Tabetic Crises. A. Radovici and N. Wertheim.—p. 754.

**Human Brucellosis Treated with a Combination of Streptomycin and Sulfadiazine.**—Janbon and Bertrand treated 32 patients with infection due to Brucella melitensis with a combination of streptomycin and sulfadiazine. The two drugs were administered simultaneously for twenty days, streptomycin in doses of 2 Gm. in six intramuscular injections in twenty-four hours and 6 Gm. of sulfadiazine taken in 6 divided doses by mouth within the same period. There was a pronounced and constant effect of the drugs on the fever and its accompanying symptoms. The hepatosplenomegaly was improved. The effect of the treatment on the various local manifestations of brucellosis varied. The treatment was ineffective with respect to osteoarthritis and the meningoneurologic syndromes. Blood cultures became negative in only two thirds of the cases and relapses were observed in some of them. In early cases in which treatment was instituted within the first three months of the disease, recovery resulted in 10 of 23 cases (43.5 per cent). This result is definitely inferior to that obtained with specific intravenous vaccine. Results were poor in cases of long standing. Treatment was ineffective with respect to the chronic manifestations of the disease, which persisted although the temperature was restored to normal. Relapse occurred within sixty days in the cases with unfavorable results. Urinary lithiasis caused by sulfadiazine was observed in 5 cases and required premature discontinuation of the drug in 2 cases.

**Electroshock Treatment for Intractable Pain.**—Radovici and Wertheim treated 2 women, aged 36 and 50, with traumatic causalgia of the left hand, 1 woman aged 50 with coccygodynia, 1 man aged 41 with tabetic crises and 10 morphine addicts with intractable pain, by electroshock. Pain subsided in all patients for ten to fourteen days and was less severe on recurrence. The authors believe in the concept of the mechanism of pain according to which pain is associated with a disturbance of the humoral equilibrium, the regulating center of which is situated in the diencephalon. Although the mode of action of electroshock is not completely understood, it is possible that the electroshock brings about an alteration in the humoral equilibrium. This method of treatment for intractable pain seems to be justified. It is preferable to mutilating neurosurgical procedures, such as prefrontal lobotomy or chordotomy.

## Schweizerische medizinische Wochenschrift, Basel

**79**:685-704 (July 30) 1949. **Partial Index**

*Oil Pneumonia Following Prolonged Use of Liquid Paraffin in Nose Drops. P. H. Rossier and A. Bühlmann.—p. 685.
Effect of Active Forms of Atmospheric Oxygen on Man. M. Curry. —p. 686.
Encephalitis Following "Q Fever." T. Wegmann.—p. 690.
*Heredity of Otosclerosis. U. Pfändler.—p. 692.

**Oil Pneumonia After Prolonged Use of Liquid Paraffin as Nose Drops.**—Rossier and Bühlmann cite the case of a woman, aged 50, who complained of cardiac symptoms and increasing dyspnea on exertion. Roentgenoscopic examination revealed diffuse shadows of both lower pulmonary fields. Percussion and auscultation revealed dulness that increased in the downward direction; bronchial respiration and rales could likewise be detected. Questioning revealed that the patient had used an oil spray for a dry rhinitis for more than twenty years and since 1940 she had frequently dropped into her nose, by means of a pipette, liquid paraffin that contained an admixture of aromatic oils. She had used about 150 cc. per week, a total of about 64 liters. The sputum contained many fat droplets. The greatly reduced vital capacity was increased following an injection of epinephrine, probably because the dyspnea was partly due to the spastic reaction of the bronchi to the foreign body stimulus. This suggests therapeutic possibilities. This case again proves the danger involved in the application of oily substances in the upper repiratory passages.

**Heredity of Otosclerosis.**—Pfändler states that during the past two decades most geneticists have assumed that there is an irregular dominance, with perhaps simple recessiveness, for otosclerosis. Geneologic investigations and detailed clinical studies on an extremely prolific farmer family in Switzerland, which had lived in the same region for centuries, and in which there had been consanguineous marriages, indicated that otosclerosis is a distinct and characteristic nosologic entity, which is brought on by a genetic mutation with dominant character. It is believed that in the heterozygous state otosclerosis rarely becomes manifest; if it does, it is less severe and appears only at an advanced age. This is explained by the extremely variable expressiveness and the feeble penetrating power of the involved hereditary factor. Even when the factor does not manifest itself clinically for several generations, this does not justify the assumption of a recessive heredity because the histologic examination of the organ of hearing reveals the existence of otosclerotic foci in about 10 per cent of the population. The recessive heredity which seems to manifest itself in certain family strains is only apparent; in reality this is a heterozygous manifestation of a factor which can be detected only in histologic preparations. The clinical manifestation of heterozygous otosclerosis can be influenced by exogenous factors and also by the endogenous milieu. This signifies that the expressiveness of a gene conditioning heterozygous otosclerosis can vary according to strains and families. In case of association of two allelomorphic genes conditioning otosclerosis, a homozygous manifestation of the disease occurs, which then becomes manifest in a severe form and at a relatively early age. Even if homozygous otosclerosis expresses itself in a regular manner and at a relatively early age, according to the indications in the family strain reviewed here the severity and the age at which it appears can vary with the endogenous milieu. Simple otosclerosis is produced by a genic mutation different and independent from those which produce recessive deaf-mutism and dominant labyrinthine deafness. The otosclerosis which expresses itself facultatively in the syndromes of Marfan and Hurler as well as in progressive lipodystrophy, certainly has a genetic origin which is entirely different from those which explain simple otosclerosis. It is possible to admit the existence of different mutations, all of which condition otosclerosis. It can be a matter of multiple allelomorphism or disturbances influencing genes of diverse localization. Otosclerosis is truly homozygous only if there is a consonance between two allelomorphic genes.

# Book Notices

THE REVIEWS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES AND DO NOT REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED.

**The Costs of Health Insurance.** By George Soule. Paper. Pp. 27. Committee on Research in Medical Economics, Inc., 1790 Broadway, New York 19; Public Affairs Institute, 312 Pennsylvania Ave., S.E., Washington, D. C., 1949.

This book constitutes a study of the economic aspects of national health insurance by an economist who is credited with some renown in his field but who takes the liberty of showing only one side of the picture.

The author uses facts and figures generously, but usually to serve his own purpose, and he ignores any and all items which might lead to doubtful or negative impressions of his own ideas. The author considers several cost estimates of health insurance and concludes that the most reliable figures available are those of the Bureau of Research and Statistics of the Social Security Administration. These and other government figures provide the basis of his study.

From the standpoint of cost in terms of money, the author states that the proposed program amounts to a redistribution of the burden of existing cost, and only additional medical service would give rise to additional cost. He also maintains that doctors as a whole have sufficient extra time to provide 25 per cent more service, and hospitals have enough unused space to provide somewhat under 35 per cent more service. The study implies that extra service would immediately become available under the new system. Mr. Soule concludes his consideration of money costs by saying that health insurance would cost less than half a cent out of every dollar spent, and the relevant question is whether the citizens want the system that much.

Next, consideration is given to the cost in terms of manpower and goods, and the conclusion is reached that such cost would be slight during a period of full employment. The extra cost of additional medical services is to be paid out of the increased product of future production. The following point made by the author should be of interest to the medical profession: "It is likely that in the future a considerable expansion in employment opportunity in medical service would fit very nicely with some decline in the need for manpower in the industries supplying material goods."

The effect of bad times on the proposed program is the next item, and the author states definitely that the plan would be financed by taxes. Decreased payroll taxes would therefore affect operations, and in the event of a severe or long-continued depression revenue would not be adequate. The deficit would have to be met by federal appropriations borrowed from general funds, but since such funds do not come out of current income and do not reduce spending, the effect would be to enlarge demand and stimulate employment. The author's primary conclusion is as follows: "Health insurance tends toward stabilizing purchasing power among the mass of the people. It tends to emphasize larger spending and smaller saving during depressions, and this is desirable because employment is thus bolstered."

Final consideration is given to who would bear the cost. The author feels that any new payroll taxes on employees for health insurance would not be an added burden to the low income group since it would be less than their present average output for medical care, that the tax on employers would usually be passed on to consumers and that federal contributions are likely to be small and would come largely from income tax revenue.

Since the author is not making a comparison study, he is left in the fortunate position of not having to say whether costs would be greater or less or the program more effective than any other plan or program, nor does he have to compare advantages or disadvantages. He presents his own estimates, draws his own conclusions and implies that the results are good—but on the basis of what?

**Ernia del Disco e sciatica vertebrale.** Di Francesco Delitala, direttore dell'Instituto Rizzoli di Bologna, e Augusto Bonola, primo aiuto dell' Instituto Rizzoli. Paper. Price, 1800 lire. Pp. 213, with 108 illustrations. L. Cappelli, Via Farini 6, Bologna, 1949.

This book represents the latest Italian concept of the important subject of herniated disk and "sciatica." The senior author is the leading orthopedic surgeon of Italy, having succeeded to the top rung on the death of Professor Putti.

The authors pay tribute to the monograph of Vittorio Putti entitled "Lumba Arthritis and Vertebral Scietica," which summarizes thirty years of clinical experience. They have followed in the footsteps and have sought with their own writings to record his progress and observations of the last ten years. If death had not occurred at the height of his career, he would have undoubtedly concluded his research on "sciatalgia" due to herniated disk.

This monograph was started five years ago. The authors have become cautious in the diagnosis because not all sciatica and lumbago is attributable to herniated disk. They believe that the label of rheumatic sciatica is a cover-up for ignorance. They have restricted the use of myelography because they believe it is not entirely innocuous to put an iodized liquid in contact with the nerve roots.

Delitala states that operation is the best treatment for herniated intervertebral disk, as all other forms of treatment yield only temporary relief. The longer the delay in operating, the more serious are the consequences because of pressure on the nerve roots. Plaster of paris casts for immobilization of the spine hasten the paralytic phase. Delitala realizes that an occasional cure does occur spontaneously, but a protruded disk with acute subjective and objective symptoms demands early operation.

The authors reviewed 7,000 cases of arthritis and "sciatica" that have been treated at the Rizzoli Institute for Orthopedic Surgery. They have operated on 217 patients, and 170 of them have been followed over a period of many years. The results were excellent in 34 per cent of the cases. There were no recurrences. Results were satisfactory in 31 per cent of the cases, fair in 25 per cent and mediocre in 8 per cent. Slightly over 1 per cent of the patients received no benefit whatsoever. From this analysis, the authors feel their optimism is warranted.

The authors have studied the mechanism by which protrusion of the intervertebral disk may be determined experimentally. They believe that when the subject passes from the horizontal to the vertical position, the nucleus pulposus is subjected to a pressure of 45 Kg. When the subject passes from flexion to extension, the nucleus pulposus sustains a pressure of 90 to 127 Kg. They consider the neurologic examination to be the basis of the diagnosis and pay tribute to Professor Neri, consulting neurologist of their institute.

In the treatment, they have substituted the extradural for the intradural route, thereby rendering innocuous a procedure which formerly was otherwise.

Complications such as cerebrospinal fistulas or suppuration did not occur in any of the cases. Occasionally a mild, temporary meningism was observed.

There is an interesting illustration of the apparatus that Delitala designed for operating on these patients in the sitting posture. He also describes and illustrates the position of the patient on the operating table and the various instruments which he has found helpful. The technic of myelography is described and illustrated well. There is an extensive bibliography.

**Geriatric Medicine: The Care of the Aging and the Aged.** Edited by Edward J. Stieglitz, M.S., M.D., F.A.C.P., Attending Internist, Suburban Hospital, Bethesda, Md. Second edition. Cloth. Price, $12. Pp. 773, with 180 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1949.

"What is geriatrics?" is a question of increasing insistence.

Dr. Stieglitz is a pioneer and a leader in geriatrics. He was associate clinical professor at Rush Medical College, was the first consultant on gerontology in the United States Public Health Service and now is in active practice in and about Washington, D. C.

The first edition of this book, published in 1943, laid down foundations, stated principles and made a comprehensive presentation of clinical subjects designed to aid the physician in his daily work. This second edition, edited by Stieglitz and written

by himself and forty-six others, has preserved the outstanding essentials of the first and has added new features which further explain, stimulate and inform. The most significant change is in the subtitle, in which Dr. Stieglitz broadens the term geriatric medicine, interpreting it as the "Care of the Aging and the Aged." Thus he emphasizes that medical care includes the care of the man in addition to the treatment of his illness. The first section of the book is devoted to the nature and processes of aging and to the peculiarities, conditions and states of the body and mind that are met in persons who are old, both in health and illness. This supports and guides the physician in his clinical efforts of diagnosis, cure, care and rehabilitation. This first section includes the biologic aspects of aging; the rate of aging; anatomic, physiologic and psychologic age; the chemistry of aging; political, social and economic implications, and industrial and cultural factors.

Dr. Stieglitz's clinical applications follow, with curative methods and preventive, palliative and constructive measures. He stresses the various ways in which old persons are peculiar —notably in their reactions, symptoms, methods of repair, homeostasis, the onset of disease and its progress and consequences.

Anton J. Carlson provides a notable account of the physiologic processes of normal aging and F. D. Zeman the medical care of the "normal" aged. The principles of surgery, anesthesia and physiotherapy are presented by competent authors. All the clinical chapters are rewritten and brought up to date.

The chapter on angina pectoris and myocardial conditions by Walter S. Priest is a condensation of recent progress well supported by chapters on the normal senile heart and disturbances of conduction and rhythm.

New chapters on a genitourinary system and the nephropathies by Stieglitz and S. T. Kimble follow with diseases of the ureters, bladder and urethra by Frank Hinman Sr. and Frank Hinman Jr. A new chapter on geriatric gynecology is written by E. C. Hamblen.

The author stresses medical service to the aged in the prevention of illnesses, the retardation of progressive deterioration, prolonged invalidism and "parasitic uselessness." He does not claim to have the final answers, but he does open pathways of progress. He states, "The rewards of geriatric medicine are great, though perhaps less dramatic than those in other fields of practice. . . . There is an intense and lasting satisfaction in solving obscure complicated geriatric problems and correlating subtle psychic and physiologic mechanisms and processes and in applying prophylactic and constructive medicine to mature adults whose appreciation and comprehension of our efforts exceed those of any other age group." He does not see geriatrics as a specialty in the usual sense, and he expresses the hope that it will never be so limited. Geriatric medicine is the application of the understanding of aging to all departments of medicine. It is needed by all who see older patients, whether general practitioners or specialists. This book will be valuable to all who are interested in life guidance of the aging, which includes everyone. He has made an earnest and skilful endeavor to provide both specialist and general practitioner with knowledge, stimulus and vision that will aid in giving that service.

**Regional Ileitis.** By Burrill B. Crohn, M.D., Consulting Gastroenterologist, Mount Sinai Hospital, New York. Cloth. Price, $5.50. Pp. 229, with 74 illustrations. Grune & Stratton, Inc., 381 4th Ave., New York 16, 1949.

This small volume represents a brief review of regional ileitis by one of the pioneer students of this disease. The author reviews the many theories that have been advanced to explain the etiology of regional ileitis, but points out that the cause is still unknown. The pathology and symptomatology are then discussed along with the roentgen picture of this disease. He points out that many of these patients give a history of rectal abscesses or fistulas and that diarrhea is the most common symptom and is found in 85 per cent of the patients. Of importance on physical examination is the presence of an abdominal mass or a fistula in a previous laparotomy incision. The so-called string sign is the characteristic feature of the roentgenologic appearance of the disease.

The author outlines the medical treatment of regional ileitis but questions whether there is ever an indication for medical treatment of this disease, and one is inclined to agree with his suggestion that many of the surgical failures may be traced to procrastination in the institution of surgical treatment. The author then reviews the trend of opinion regarding the various types of surgery which have been employed for the treatment of regional ileitis and indicates that ileocolostomy with transection of the ileum proximal to the diseased bowel is the present treatment of choice at Mount Sinai Hospital. This present treatment is apparently based on a review by Garlock and Crohn in 1945 of 57 patients in whom this procedure was carried out with no deaths and a 10.5 per cent recurrence rate. These patients were followed for two to fourteen years, and it is possible that some of the more recently treated patients may yet develop a recurrence. It is also possible that patients who were subjected to a one and two stage resection had a more extensive form of the disease. In the 55 patients subjected to a one stage resection of the diseased ileum and right colon there were 9 deaths; there were 2 deaths in 16 patients who had a two stage resection. No doubt this high mortality rate is associated with the fact that in a large general hospital such as Mount Sinai many of the cases are late cases and, because of this, poor operative risks. The book is written in an interesting manner and is extensively illustrated. This book does not propose to be a reference volume on regional ileitis but a relation of personal experiences and deductions drawn from these experiences.

**Diseases of Children. Volume II.** First edition edited by Sir A. E. Garrod, K.C.M.G., D.M., F.R.S., Frederick E. Batten, M.D., M.A., F.R.C.P., and Hugh Thursfield, D.M., M.A., F.R.C.P. Fourth edition edited by Donald Paterson, M.D., F.R.C.P., Consulting Physician, Hospital for Sick Children, Great Ormond Street, London, and Alan Moncrieff, M.D., F.R.C.P., Nuffield Professor of Child Health, University of London. With contributions by twenty-four contributors. Cloth. Price, $10. Pp. 1033, with 380 illustrations. Williams & Wilkins Company, Mt. Royal & Guilford Aves., Baltimore 2, 1949.

This is the second volume of a new two volume edition of this well known British textbook. The majority of the twenty-four contributors, all of whom are leaders in British pediatrics and its allied specialties, are associated with the Hospital for Sick Children, Great Ormond Street, London.

Eleven chapters are devoted to thorough descriptions of the major diseases, grouped according to anatomic systems. In addition, there are seven chapters dealing with congenital mental defects, orthopedic surgery, urologic surgery, rheumatic fever, infectious diseases, venereal diseases and malignant conditions. Special sections are devoted to encephalography, electroencephalography, mental testing and congenital heart disease. The book is admirably illustrated and the material conveniently arranged. Each section is followed by a short list of references.

In general, this is a remarkably complete textbook for its size. In this respect, its scope lies between that of the average American pediatric textbook and Brennemann's system of pediatrics. The inclusion of sections on pediatric surgery and on such special fields as dermatology and ophthalmology is particularly valuable. There is an extensive treatment of diseases of the nervous system, occupying approximately one quarter of the book, in which a chapter on functional disorders of the nervous system presents useful information frequently missing from pediatric textbooks.

However, the American reader will find occasional instances where British experience or terminology appear to differ considerably from the American. There is more emphasis on morbid anatomy and less on pathologic physiology and chemistry than would normally be expected. The surgical treatment of Wilm's tumor is reported as "universally disappointing." Surgical treatment of cranial synostosis is not mentioned. Tuberculous meningitis is the commonest form of meningitis in England. In the sections on therapy, which often seem too brief, the American reader is at a disadvantage because of the frequent use of British proprietary drug names.

While these minor criticisms may reduce the usefulness of the book for the American medical student, they do not detract from its excellence as a general pediatric textbook. This new edition carries on the fine traditions of an internationally famous textbook of pediatrics, characterized by that felicity of language which so often distinguishes British medical literature from the more pedestrian prose of American medical writing.

# Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

## NEPHRITIS FOLLOWING A MISCARRIAGE

*To the Editor:*—A white woman aged 28 had a miscarriage seven months ago. Fatigue, swelling of the tissues and albumin (4 plus), casts and blood cells in the urine appeared during pregnancy. The swelling disappeared shortly after the miscarriage, but the albumin, blood cells and casts remain. The quantity of albumin varies greatly. Tests taken only a few hours apart will vary from a mere trace of albumin to a 4 plus reading. The tests reveal the least amount—at times perfectly clear—during menses. The patient has been placed on a salt-free diet; moderate rest and vitamins have been prescribed. What can be done to discover how much the kidneys have been damaged and whether such damage is permanent? How can one determine whether the damage is in the upper or lower tubular region? Does the liver have an important effect in such cases? What possible meaning can be drawn from the clear tests during menses? What treatment is recommended for this patient?

J. E. Allgood, M.D., New Middletown, Ohio.

ANSWER.—The history suggests that acute glomerulonephritis developed during the pregnancy of the patient. This diagnosis would be made more probable by knowledge of a preceding upper respiratory infection and some elevation in blood pressure. It is assumed that her urine was normal prior to the pregnancy; otherwise an exacerbation of a previous mild or latent chronic glomerulonephritis may have developed. Variations in volume or salt content of the urine, in posture or activity, may give rise to fluctuations in the amount of albumin. If the patient spends more time resting during her menses and her renal circulation is favored thereby, the concentration of protein in the urine may diminish considerably.

Her renal function should be determined by a urea clearance test or by a fifteen minute fractional phenosulfonphthalein test. Orthostatic proteinuria should be carefully excluded. There is no clinical way of determining whether the damage is chiefly in the upper or lower nephron; even with complicated investigative procedures this may be impossible, since changes in function in the upper part of the tubule may prevent the lower segment from receiving the proper urinary fluid on which to act.

The liver is not involved in nephritis except so far as independent impairment of hepatic function may reflect itself in insufficient destruction or neutralization of hormones from the posterior pituitary or adrenal cortex which can act on the renal tubule to an excessive degree. This would be manifested chiefly in delayed salt and water excretion or edema. The liver may also be a factor in postural proteinuria because of the relationship of the inferior vena cava to the undersurface of the liver, and because of possible compression by traction on the vein in the upright position.

In the absence of edema and of low plasma albumin level, there is no good reason for a salt-free diet. The patient's diet should be normal if renal function is reasonably good. Chemotherapy and antibiotics are indicated only in the presence of demonstrable infection. They have no beneficial effect on the nephritis itself unless one is dealing with an infection due to acid-fast organisms.

## PREPARATIONS FOR PREVENTING SUNBURN

*To the Editor*—What information have you concerning the addition of iodine to protective oils? What preparation would you suggest for use in protection of the skin against undue exposure to the sun?

William C. Buss, M.D., Bakersfield, Calif.

ANSWER.—Preparations designed to prevent sunburn usually contain phenyl salicylate, 10 per cent; quinine, 15 per cent; tannic acid, 2 per cent, or para-aminobenzoic acid, 15 per cent. According to Schwartz and Peck (Cosmetics and Dermatitis, New York, Paul B. Hoeber, 1947, p. 144) phenyl salicylate and quinine are seldom used now because they are cutaneous sensitizers. They recommend a lotion containing isobutyl-*p*-aminobenzoate, 5 per cent, alcohol, 60 per cent, glycerine, 10 per cent, and water, 25 per cent. The addition of 2 per cent tannic acid to this formula will help to simulate suntan and to increase the sunburn-preventive action. Para-aminobenzoic acid, 15 per cent in a greaseless base, is also effective. When iodine is incorporated in such preparations, it is usually for the purpose of coloring the skin to simulate suntan. In sufficient concentration it would irritate the skin.

## LAMINECTOMY AND SCIATICA

*To the Editor:*—In what circumstances is laminectomy for sciatica indicated? About what percentage of cures may be expected from the procedure? What may account for the operations that are not successful? How long are patients usually hospitalized for such an operation? Not including the laminectomy, what is considered the latest and most successful form of therapy in sciatica?

M.D., Virginia.

ANSWER.—Sciatica is not a disease entity but a symptom complex, due to many different circumstances. Laminectomy is indicated when a definitely protruding disk, usually between the fourth and fifth lumbar vertebrae or between the fifth lumbar vertebra and the sacrum, can be demonstrated. A positive diagnosis is usually possible by means of spinal fluid analysis for total proteins. Careful neurologic examination often reveals an absent ankle jerk on the affected side, and characteristic sensory changes may occur. Roentgen examination with an opaque material in the spinal canal may also demonstrate the exact location of the pressure point. In such circumstances laminectomy with removal of the protruding disk is successful in relieving the pain in a high percentage of cases. Lack of success with positive diagnostic criteria usually results from failure to find or remove all the protruding disk or disks and from recurrence of the disk protrusion. Hospitalization for simple laminectomy and disk removal, without fusion, is usually not longer than two weeks. It is not possible to state what the successful treatments for sciatica are, other than laminectomy. Because of the variety of causes, a careful and intensive search and accurate diagnosis should precede any attempt to treat sciatica. A few other causes of sciatica are tumors, true neuritis due to infections or nutritional disturbances, spondylolisthesis, tuberculosis, brucellosis, syphilis, herpes zoster, psoas abscesses, gluteal fibrositis, bursitis, tight iliotibial band, foot strain and faulty posture.

## DREFT® AND PEPTIC ULCER

*To the Editor:*—What is the present status of dreft® in the treatment of peptic ulcer? Is the sodium in this compound absorbed? Would use of this compound be contraindicated in a salt-free diet? One of my patients, a man aged 45, has had good results with symptomatic relief of a peptic ulcer through the use of the product, but recently, because of hypertensive and coronary arteriosclerotic heart disease, I have prescribed a considerable degree of sodium restriction. Because of this, he discontinued the use of dreft® and his ulcer symptoms have become troublesome again.

M.D., California.

ANSWER.—Dreft® is composed principally of sodium lauryl sulfate. Assuming that all the sodium is utilized in the body, 1 Gm. of sodium lauryl sulfate would supply 80 mg. of sodium ion, whereas 1 Gm. of sodium chloride would supply 400 mg. of sodium ion. With the dosage usually employed (0.2 Gm. sodium lauryl sulfate every two hours), this amount of sodium would be negligible in the diet if it were all absorbed.

The use of sodium lauryl sulfate has largely been abandoned in the treatment of peptic ulcer. Although it inactivates pepsin, it also produces degenerative change in the intestinal mucosa, liver and kidneys. Furthermore, by inactivating the pepsin it interferes with proper digestion of protein and thus accomplishes its benefit at the expense of the destruction of a normal physiologic process.

## LITHIUM POISONING

*To the Editor:*—What are the possible after-effects of acute lithium poisoning?

M.D., Washington.

ANSWER.—Adequate information on the mechanism of lithium poisoning or its residual effects still is lacking. It is not possible, precisely, to claim that the lithium ion per se is highly toxic or instead that by replacing the electrolytic action of either or both sodium and potassium it upsets physiologic economy within or between the two major partitions—the intracellular and the extracellular phases of water balance. Until the appearance of additional data, all opinions should be cautious. From recent episodes in human beings, two features appear to be well established: (1) the usual victim of high lithium intake already is so direly ill that little demarcation may be drawn between manifestations of already existing disease and the peculiar actions of lithium; (2) in milder instances the withdrawal of lithium appears to have been followed by early cessation of any untoward action. The implication is that no continuing action persists. Although lithium may be briefly stored, it is established that lithium is eliminated both through the intestinal tract and the kidneys. In the case of renal elimination there is scant evidence of damage, although this has been claimed. On a speculative basis, two items of possible pure lithium action are most likely to have residual effects: (1) depressed spermatogenesis or at least depressed spermatozoal motility may be prolonged, and (2) accumulated

abnormal body fluids, such as ascites with a lithium chloride content, may not readily be physiologically removed. The body does not store ordinary water. Always there must be an electrolyte. If lithium has replaced sodium, absorption may be hampered. In general, the trend of the moment is to believe that specific after-effects are few, if any, after the lithium has been eliminated.

## HEPATIC CIRRHOSIS

*To the Editor:*—**A 53 year old white man has cirrhosis of the liver of about six years' duration, with abdominal ascites, requiring paracentesis at weekly intervals. He has pitting edema (2 to 3 plus) of the legs up to the hips, without sacral edema, although on a regimen of strict bedrest. This is complicated by mitral stenosis, the heart being greatly enlarged to the left with apical systolic murmur and regular sinus rhythm. The lungs have always been clear. Digitalization produces better heart tones and more regular rhythm with some slowing of the rate, but it does not affect the edema. There is definitely increased venous pressure, as the external jugular veins are filled in a semisitting position, yet I believe that he has primary cirrhosis of the liver, with the edema resulting therefrom. The mercurial diuretics do not produce diuresis. What results may be expected from the so-called button operation (planting a glass button in the abdominal musculature)?**

**M.D., Washington.**

ANSWER.—The button operation proposed by Crosby and Cooney consists of the insertion of a modified Murphy button into the abdominal wall connecting the peritoneal cavity with the subcutaneous tissues. This provides for free drainage of the ascitic fluid into the subcutaneous tissues, where theoretically it is easily absorbed. The original results of this procedure were believed to be favorable, but recently Chalmers and Davidson published a discouraging report (*New England J. Med.* 240: 449, 1949). Of 14 patients on whom this operation was performed, 5 died in the postoperative period, and of the 9 who survived 4 had recurrence of ascites within one month, 3 within three months and 1 within fourteen months. Nine of the whole group were examined post mortem, and in these no functioning buttons were found. In 4 there was plugging with fibrin and in 3 with omentum. Chalmers and Davidson reported, as did Welch (*New England J. Med.* **237: 735, 1947**), the formation of subcutaneous pockets lined with dense, hyalinized connective tissue from which little absorption could occur. The aforementioned reports raise serious doubts as to the value of this procedure. Lord (J. A. M. A. **136: 767,** 1948) has modified the operation by stripping the fascia from the muscles of the abdominal wall over a large section adjacent to the external opening of the button; he reported good results in 1 case, but no further experience with this type of operation has been reported as far as could be ascertained.

One would hesitate to recommend surgical approach to the management of ascites in your patient without knowing more about the venous pressures and values for serum albumin. Has constrictive pericarditis been excluded? Is there evidence of disturbed hepatic function? A salt-poor diet of the type described by Chalmers and Davidson (*New England J. Med.* **240: 449,** 1949) should be tried as a preliminary measure, and perhaps the use of salt-poor human serum albumin also would be helpful.

## UNDESCENDED TESTES

*To the Editor:*—**What is the proper time to use gonadotropic hormone for undescended testes? Should it be used as early as possible, and should it be used at all in cases in which the testes occasionally descend and then are pulled back again into the canal?**

**William Sulman, M.D. Hazleton, Pa.**

ANSWER.—Accurate diagnosis is important in the treatment of undescended testes. Migratory testes—those which move back and forth from the scrotum to a higher level—are not true undescended testes and do not require treatment. The diagnosis of undescended testis should be made only when it is impossible to displace the testis into the scrotum on repeated examination. When true cryptorchism is present, treatment should be started by the third year of life if possible. Chorionic gonadotropin should be administered intramuscularly in a dose of 500 international units three times a week for a period of six to eight weeks. With this treatment, descent occurs in about 25 per cent of the cases. If the testis does not move into the scrotum after treatment has been given in this manner for eight weeks, the defect should be corrected surgically.

Glandular therapy should be continued to the time of operative intervention. If it is stopped, some atrophy of the genitalia will occur, which increases the technical difficulties of the surgical procedures. Chorionic gonadotropin should not be administered for a long period of time in young children. Only enough treatment should be given to induce a small amount of genital growth. If the substance is given over a long period of time, a condition resembling precocious puberty will develop.

## LUPUS ERYTHEMATOSUS

*To the Editor:*—**A 35 year old white woman had maculopapular erythematous lesions in the exposed V of the neck six years ago. The lesions gave the sensation of "crawling" and itched, particularly as they began to appear. The appearance of the lesions seems to bear a direct relationship to exposure to the sun, appearing in the spring and disappearing in the fall without scarring or pigmentation. The skin has remained free of the eruption every winter. This spring the lesions appeared for the first time in the left malar region, with few lesions on the neck. Several lesions also appeared on the forearm. Those on the face became confluent and covered an area 8 by 3 cm. A dermatologist made a biopsy of one of the lesions, and a pathologist diagnosed the condition as lupus erythematosus. The patient has had no fever, and she appears to be in good health. There have been no signs of serositis (polyarthritis, pleuritis or pericarditis). The urine has always been normal. Is a diagnosis of lupus erythematosus warranted on the basis of the histologic picture alone, in the absence of clinical signs? If this is lupus erythematosus, what is the prognosis? Can lupus erythematosus confine itself entirely to the skin, without other systemic involvement? What is the present accepted treatment of lupus erythematosus?**

**M.D., Wisconsin.**

ANSWER.—It is frequently difficult to distinguish between solar dermatitis and superficial lupus erythematosus. In such cases one must resort to biopsy, for the histologic picture of lupus erythematosus is a characteristic one and experienced pathologists recognize it readily. The disease—as does discoid lupus erythematosus usually—may occur on the skin only without systemic manifestations. Nevertheless, the prognosis must be guarded in the superficial erythematous type of lupus erythematosus, which is adversely affected by sunlight. The treatment is usually with heavy metal preparations, such as gold, bismuth or arsenicals; vitamin E; para-aminobenzoic acid; calcium pantothenate; quinine, and iodoform. They all have their advocates. If possible, any foci of infection that are present should be eliminated. The patient should avoid not only sunlight but wind and cold as well. For topical use the patient should apply a sun screen ointment, such as para-aminobenzoic acid, 15 per cent, in a greaseless ointment base.

## REACTION TO INDIGO CARMINE

*To the Editor:*—**A patient aged 37 received 5 cc. of sodium indigotindisulfonate (indigo carmine) intravenously during a cystoscopy. After about 2 cc. had been given slowly, the patient complained of severe frontal headache. The injection was stopped; the pulse, temperature, blood pressure and color were normal. A cold cloth was applied to the head, and the injection was slowly continued. The patient continued to complain of excruciating pain in the entire head, neck and shoulder muscles. Sedation had only temporary results. Repeated checks of blood pressure, pulse and temperature revealed that they were within normal limits. She was sent home and had a restless night. Next day the headache persisted and she vomited twice. Eight to ten tablets of acetylsalicylic acid, two tablets of a proprietary headache remedy, and 2 grains (0.13 Gm.) of phenobarbital were required to give her relief. The second and third days did not show any let up. She vomited repeatedly. She was sent to the hospital, and a neurologic consultation was held. An hour after 50 mg. of tripelennamine hydrochloride (pyribenzamine hydrochloride®) was given the pain improved considerably. The spinal puncture revealed normal pressure, but there were 277 red cells in the sediment. With the help of codeine, ice packs, and tripelennamine the pains were gradually subsiding. Results of a complete neurologic examination were essentially normal except for a suggestion of rigidity of neck muscles. Is this an allergic reaction caused by petechiae in the meninges of the brain? Are there similar cases on record?**

**M.D., California.**

ANSWER.—No reports of reactions to sodium indigotindisulfonate have been found in the recent literature; older reports dealt with reactions to impure preparations. The reaction described would seem to be an atypical "intravenous reaction" sometimes seen after the injection of colloid materials. Such reactions have been described by Hanzlik, De Eds and Tainter (*J. Pharmacol. & Exper. Therap.* **21: 3,** 1923; *Arch. Int. Med.* **36: 447,** 1925). Although most such reactions are characterized by a resemblance to so-called nitritoid crises, their mechanism is probably due to a sudden alteration in the colloidal osmotic pressure of the blood. The usual symptoms are excitement, anxiety, flushing of the skin, sweating, precordial distress, tremors, cough and dyspnea, vertigo, headache, nausea, vomiting, chill and fever and joint pains. However, many of these symptoms may be absent and others accentuated. It is significant that an antihistaminic agent improved the patient's symptoms, although this may have been due to the well known sedative effect of this class of drugs.

The production of petechial hemorrhage in the meninges appears as a possible explanation of the reaction, and if the spinal tap was done in such a manner as to preclude contamination with blood, the presence of red cells lends support to this hypothesis. The effects on blood pressure, pulse and respiration produced by intravenous injections are usually fleeting in character and may pass undetected. Usually, if immediate death does not occur, recovery from these intravenous reactions is complete.

## OLEANDER POISONING

*To the Editor:*—On July 21 a soldier came to the sick bay after intense vomiting of 30 minutes' duration which became so severe that he vomitted blood. He had one watery stool in that time. He was tugging at his clothing and attempting to remove it, saying that he felt as though he were "burning up." His skin showed pallor, which was further emphasized by cherry red lips. His skin was cold and clammy with profuse perspiration. His pulse rate was 124; his respirations were rapid and labored, and his temperature was 99 F. He claimed that he had no pain. The patient stated that a few minutes prior to coming to the sick bay he was waiting for his wife outside his home. He picked a flower from an oleander bush and placed the stem between his teeth, getting the fluid on his lips and in his mouth. The taste was exceedingly bitter. Fifteen minutes later the foregoing symptoms started. Rest but no medication was prescribed, and the condition subsided considerably in about two hours, but he was restless; he was given morphine ¼ grain (15 mg.). He awoke next morning feeling well and returned to duty. I believe that this was a case of oleander poisoning. I would appreciate any information or reference to literature on this subject.

Thomas G. Lyons, M.D., Litchfield Park, Ariz.

ANSWER.—Oleander has been used for many years in southern Europe as a rat poison, against which species its action is similar to that of squill. The active principle of oleander is a glycoside oleandrin, also known as folinerin, which hydrolyses into gitoxigenin. This substance is also produced by hydrolysis of gitoxin, one of the glycosides of digitalis. Other principles, chiefly glycosides, have been isolated from oleander. The principal actions of oleander resemble those of digitalis; it has been used in Europe as a substitute for the latter drug (Pouloux, *Bull. gén. de thérap.*, May 15, 1888; Freiherr, *Arztl. Rundschau*, 1899).

A number of cases of poisoning have been reported in the older European literature. The symptoms have been vomiting, abdominal pain, dilatation of the pupil, vertigo, convulsive movements, insensibility and a weak, slow pulse.

Although the symptoms described in the case reported do not resemble those reported in medical literature, the dose received was far less than that in the European cases. Furthermore, the presence of other, as-yet unidentified, constituents could have masked the predominant digitalis-like actions. In the case cited the predominant actions were on the peripheral vessels with possible vasodilatation, fall of blood pressure (hence, rapid pulse rate) and compensatory constriction of skin vessels. It is reported that one or more of the principles of oleander exert effects on cardiovascular and respiratory centers in the medulla; hence, some of the symptoms may have originated centrally.

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## CANCER OF THE COLON

*To the Editor:*—A patient aged 67 had a colostomy in 1947. The surgeon who operated on the patient said he had cancer of the lower part of the colon. Resection was refused. The man has had paralysis agitans for twelve years. Except for enlargement of the cancer area (seen by roentgenogram) there is no roentgenographic evidence of spread in the gastrointestinal tract and chest. The blood cell count and urine are normal. It is debatable whether masses are palpable in the abdomen. Roentgenograms of the skull and spine were not taken. Reflexes are normal. The patient is getting each day: 1 grain (65 mg.) of codeine by mouth, 1½ grains (98 mg.) of tuinal[3] (a mixture of equal parts of amobarbital sodium and sodium 5-allyl-5-[1-methylbutyl] barbiturate) and 25 mg. capsules of diphenhydramine hydrochloride twice a day (for urticara). About three nights ago, he went into coma, during which his respirations were shallow and about 1 every 75 seconds and the heart beat was weak and slightly irregular. Deep pressure over the eyebrows brought no response. His medicaments had been unchanged for the previous two months. This condition was present about an hour before I was called and for twenty minutes of my observation. I gave him 1 cc. of aqueous epinephrine intravenously along with 1 cc. of epinephrine in oil intramuscularly, and in five minutes he was responsive. At present he is getting along fairly well.

Henry Sydow, M.D., Albion, Neb.

ANSWER.—The diagnosis of a long period of fainting or a short period of coma in a debilitated patient occurring without obvious cause with recovery because of (or simply after) injection of epinephrine is little more than a guess. Among the many possibilities one thinks first of temporary interference with cerebral blood flow. Such interruption occurs commonly and evanescently as a part of the "small stroke" picture, the loss of consciousness probably being caused by reflex vasospasm attendant on a small cerebral accident rather than on ischemia peripheral to the lesion itself. The associated weak and irregular heart beat, however, lends support to the concept of a cardiac mechanism for the cerebral ischemia, rather than a local one. Such attacks occurring classically in the Stokes-Adams syndrome, with complete auriculoventricular block, also are observed at the onset of other disturbances in mechanism, such as transient auricular fibrillation, flutter or the paroxysmal tachycardias. Carotid sinus syncope is another possibility. From the data presented, a temporary reduction in cerebral blood flow on a cardiogenic basis is regarded as the most likely possibility.

## CHILDREN'S SHOES

*To the Editor:*—I would like to comment on the answer to the question on children's shoes in The Journal, Aug. 27, 1949, page 1378. It seems to me that the answers given indicate a superficial acquaintance with the problem. The following opinions are based on records with photographs of several thousand cases of foot imbalance in children.

Walking on any soft and yielding surface is fatiguing and imposes a tremendous strain on the muscles and ligamentous structures of the feet. This is particularly true of the child who may stand for many weeks holding on to the sides of his crib or bed or play pen with all his weight borne on the yielding mattress or pad. Most adults have had the experience of walking a long distance over a soft, yielding surface, barefoot, and know that it imposes an extreme strain on the feet. This is doubly true of the relaxed ligamentous structures in the foot of a baby that is just beginning to bear weight. The average so-called baby shoe is an abomination, and wearing it is somewhat worse for the child than being barefoot. In this I refer particularly to the soft-soled type of shoe. Every baby should be put in a hard-soled shoe as soon as he begins to stand. I am familiar with all the nostalgic sentimentality with which the average adult excuses a child's going barefoot and even encourages it. I am also familiar, in my own practice, with the child who in three months of going barefoot in the summer loses all that he has gained in correction of flatfoot and knock knee in the previous nine months of wearing shoes with supports. Going barefoot may permit normal development of the normal foot; however, almost all foot difficulties in adults have a basis in hereditary anatomic variations from normal. A large percentage of adults must have some foot disability; otherwise, why all the various so-called corrective shoes, arch supports and corn plasters on the market? I agree with the statement that the infant's first walking shoes should be firm soled with a rigid counter and adequate support for the arches. I will go further; they should be hard soled, and most of them would be better if they had a small heel and a rigid shank rather than a complete absence of heel, as seen in most small children's shoes. A tightly laced shoe, such as a skating shoe, affords some temporary support to the ankle. However, it is impossible in everyday use to lace an infant's shoe this tight; even if it were laced tightly the leather would soon get out of shape and give so as to remove all supportive effect. The upper in a shoe is merely there to hold the shoe on the foot and to hold the foot squarely over the sole; this is the only advantage of a rigid counter. There are two much more practical reasons why the first shoes should be high shoes: A small child's foot has a short lever arm with which to bend the fore part of a rigid-soled shoe, and it is almost impossible for such a child to keep an oxford on his foot and walk with a normal gait, second, until a child reaches the age of 3 or 4 years he cannot be made to readily understand that he should keep his shoes on; he will remove them at every opportunity, especially if they are poorly fitted, as is the case in most shoe stores, where most shoe clerks speak glibly and with an air of authority on a subject of which they know nothing. Much harm can be and is constantly being done by shoes that are too short. Little, if any, harm other than an occasional blister is ever done by a shoe that is too large. The continuation of the sole up the back of a shoe may serve as a firm counter, but the manufacturer put it there to make the shoe more wear-resistant in an area frequently subjected to considerable abuse by growing children.

Duncan C. McKeever, M.D., Houston, Texas.

## FRIGHT AND FETAL DEATH

*To the Editor:*—In reference to the query in *The Journal* August 20, page 1344, fright has been known to cause fetal death. I endeavored to explain how it comes about in a paper on "Slowing of the Fetal Heart and Its Relation to the Fetal-Placental Circulation" (*Am. J. Obst. & Gynec.* **24**: 898 [Dec.] 1932). Slowing of the fetal heart is produced by contraction of the uterus compressing the placenta and forcing some blood out of it and into the fetus, thus increasing the volume and tension in the fetal circulation which causes the heart to slow down. If intense contractions persist, the fetal circulation is overloaded and the heart will stop beating.

When the mother suffers a nervous shock a reverse process takes place. The sympathetic nervous system is not fully developed in the fetus, and there is no evidence of the placenta being supplied with these nerves. The question arises, how is the blood pressure in the fetus and placenta maintained? The likely explanation is that the placental and fetal circulation derives its tone from the uterus. It is the tonic state of the uterus which holds the placenta in place and properly contracted. This contraction maintains the pressure in the placental circulation. This in turn is transmitted to the fetal circulation. Should the uterus, for some reason suddenly relax, pressure in the fetal and placental circulation would drop and shock would result in the fetus. This, I believe, explains how death of the fetus occurs when the mother suffers sudden nervous shock. A general relaxation takes place in all abdominal viscera of the mother. The uterus loses its tone and relaxes; this removes the tone from the placenta, and the vessels dilate. The blood from the fetus flows out into the placenta, the blood pressure drops, shock occurs, and the fetus dies.

Morris Leff, M.D., New York.